Received: 19/11/2025 | Accepted: 4/12/2025 | Published: 30/1/2026

CONTEMPORARY RESEARCH IN NATURAL PRODUCTS

Review

Optimizing Earth's Resources for Medicines Security

Geoffrey A. Cordell [1, *]

[1]Natural Products Inc., Evanston, IL, USA and College of Pharmacy, University of Florida, Gainesville, FL, USA
*Correspondence: Geoffrey A. Cordell; pharmacog@gmail.com

Edited by Khozirah Shaari, PhD

Keywords:

Sustainability
Medicines Security
Defossilization
Replacement Bioactive Agents
Degrowth

Abbreviations:

EU
SDG
4IR
GDP
CEEPO
L.O.V.E
W.A.S.T.E

ABSTRACT

Anthropogenic devastation and ignoring non-renewable resource boundaries have brought humanity to a place where the continuing experience on Earth is critically threatened. Our future depends on showing reverence for these limits, for the interconnectedness of all life on Earth, and for the continuous optimization of the remaining valuable resources. Key tipping points are close to breaching, after which no return will be possible. One, the bleaching of the coral reefs may have already been surpassed. Following numerous global meetings on climate change and biodiversity, the time for talking has long passed. Dramatic actions, including urgent defossilization, and substantial long-term financing, are necessary to rebalance the relationships of humanity within nature. The European Union (EU) says the continuous addiction to "growth" must be relinquished, "not for us but for our descendants", that their lives may have sufficiency through degrowth. This review provides a brief history of how this uncharted crisis point in Earth's history was reached and describes options for moving forward scientifically, based on contemporary thinking, for a future with sustainable medicinal and biological agents.

Humans and animals will continue to require biological agents for prophylaxis and treatment. Where will those agents originate? Beyond net-zero energy sourcing by 2050, defossilization will also diminish the foundational chemical supplies to process and manufacture synthetic and natural medicines, thereby necessitating a major paradigm shift for Medicines Security to a wholly sustainable production profile. Developing sustainable replacement reagents, sourcing, and products is a completely unexplored territory for humanity. That research paradigm shift represents an exceptional opportunity for collaborative, data- and technology-based, sustainable natural products development for the next 20-25 years. Beyond prioritized medicinal plants, innovative sourcing of chemicals will include developing agricultural and urban "(bio)waste" as a source of chemical building blocks for a new pharmaceutical industry in a circular economy that does not deplete, and may enhance, Earth's resources for future generations. Government, industry, and academia must accept that reality and commit the resources to ensure that developing sustainable medicines locally is pursued avidly, for the holistic health and well-being of the planet in which lauding an increasing Gross Domestic Product (GDP) is replaced by a focus on a holistic and healthy society.

1. INTRODUCTION

For Millennia, turning to nature has provided humanity with all that was needed to develop life as we knew it in various regions of planet Earth. That period has ended with the new reality. The marvelous web of nature, in which we are inextricably enmeshed, is breaking down rapidly. In the history of human evolution and societal development we have never been at this place where the very survival of humanity over the next 75 years is imperiled through our actions and inactions. We haven't ever witnessed an Earth which, due to anthropogenic activity, each year (each month now!) breaks a new record for the average air and the ocean temperatures, and for the rising sea levels due to the declining ice coverage in the Arctic and Antarctic regions. As the global species responsible for the current state of Earth, humanity seems unable (and unwilling!) to comprehend at a deep and responsive level the urgency that what we do and don't do in these next few years will be the most critical for our future, forever.

Whether humanity can survive and continue to thrive on a substantially resource-depleted planet will depend on the courage and the actions of a few global visionaries who have the power to think, create, and act for the future of humankind and our interwoven planet beyond the next two or three years. They must overcome the contemporary cataclysmic actions and distractions of the powerful fossil-fuel industry and those who support the drive to place transactional profit above deeper concerns for a relational future of human survival integrated within the biological systems of Earth. Actions must be taken now to care for the state of Earth in 2050 and beyond. Some global leaders are deeply concerned (derided as "alarmists") regarding this potential catastrophe for Earth. Others are actively in very deep denial, for whom climate change is the "green energy scam" and are promoting the expansion of new sites for fossil fuel development, increasing populations (pronatalism), the roll-back of environmental regulations, and consequently the expanded use of polluting, non-renewable resources. Humanistic pharmaceutical scientists have important roles to play in ameliorating, responding, researching, and educating those who can and must make a difference in this scenario for Earth and its future generations of humans.

This review provides a glimpse of the background as to where humanity stands, how we arrived here, and what will be asked of pharmaceutical scientists in the future with respect to medicinal and biological agents in a broad and non-traditional economic context. Recognizing that everything on Earth is interwoven, this discussion will cover many different aspects of what has (and has not!) happened in the past and some of the opportunities that are available for future discussion and action. Many facets of sustainability, unless there is concomitant behavioral change, maintain some of the essential elements of the *status quo*, the utilization of non-renewable resources in other economic sectors. However, contemplations and discussions regarding planetary goals, resources, and lifestyles, and the role of natural products within those frameworks for the future must be based on fundamentally different approaches.

It is essential to explore beyond sustainability and preserving what remains of the ecosystem and the UN Sustainability Development Goals (SDGs) towards zero-emissions, redefining "waste", closing the loop of a (bio)circular economy, and examining "degrowth". What regeneration plans can enhance the capacity of Gaia (not just one species!) to afford advances in qualitative wealth by embracing those development programs which will improve the remaining resources for the coming generations of all Earth's organisms [1]. First though, some background is necessary to appreciate what has brought Earth to this potent place and time, bordering on catastrophe [2,3]. The outcomes of the discussion should dramatically refocus the diverse contemporary research programs involving all pharmaceutical scientists as the future needs for pharmaceutical and biocide agents are identified and addressed at the global and local levels.

1.1 The web of life on Earth

We exist within Gaia [4]. A simple statement with profound implications. Humans (*Homo sapiens*) are one component in a large, complex living organism in which all the composite parts function as a single cohesive entity, a unifying "web", attempting to maintain a mutually beneficial homeostasis. This web of ineluctable interdependency was well-summarized in the mid-1850s by Chief Seathl (Seattle) of the Suquamish and Duwamish peoples in the Pacific Northwest. He pointed out that the strands of all life are connected, directly or indirectly, and that disturbances on one strand affect the *status quo* and modulate the interactions of the other strands of life [5]. Hundreds of years earlier, in the late 12th century, the abbess, composer, and medical naturalist St. Hildegard of Bingen (1098-1179), from a forest area in southwest Germany, had concluded that humanity was totally dependent on the natural environment "…..for without it, we cannot survive." [6]. Seemingly, humanity has not inculcated and integrated these "pearls of wisdom" (Matthew 7:6) into a series of moral life practices as our species contribution to the maintenance of Gaia [4]. Many business and government leaders still regard that somehow, humans are separate from, and can control, the other parts of nature, even when our actions (or inactions) provoke a direct response from nature that validates the profound interconnectedness. Sometimes referred to as a "war on nature" [7], our W.A.R. is in reality, the incessant dedication of humanity to "**W**asting **A**vailable **R**esources", a topic discussed subsequently.

These anthropogenic activities and incoherent and irreconcilable philosophical and practical approaches in various sectors to maintaining life on Earth are shattering the very fabric of human existence through environmental abuse and global misconduct. These accumulated activities led the well-known Harvard biologist E.O. Wilson to conclude that "Only a major shift in moral reasoning… can meet this greatest challenge" [8]. For our descendants, extending the legacy of our past, symbiotic, interwoven, mutualistic relationships is essential for the well-being and survival of the species of Earth. This enmeshed web of trophic relationships which has thrived for millennia must be honored, respected, balanced, and wholly embraced. To not do so is an abhorrent crime against the living Gaia and may abrogate a flourishing future for humanity.

1.2 The valuables of Earth

On a day-to-day basis, natural products in their myriad forms are an integral, essential, and indeed sacrosanct feature of the human experience. The list of these interactions is long, and yet, for many people, respectful and considerate contact with those natural relationships has been lost, is limited, or is tenuous. Put another way, the massive role of natural products in our daily lives is profoundly under appreciated. Perhaps this partial list will help deepen an understanding of why renewable natural resources are the cornerstone of human survival. For example, there are shelters, furniture, clothes, foodstuffs, and cosmetics. The resins, gums, and waxes that are rarely visible, and the hundreds of flavoring agents and spices which are used locally and globally. Also stimulating our senses are the perfumes and fragrances, of which the perfumes market alone is projected to be USD 62.1 bn in 2025 [9]. Prescription pharmaceuticals consistently have about a 25% natural product base, higher when semisynthetic drugs based on a natural origin are included [10]. Over-the-counter (OTC) products, phytotherapeuticals, and traditional medicines are the basis for health care globally for most humans and animals. There are the plant-derived herbicides and insecticides, the principal substances of abuse, and those plant and fungal metabolites which alter consciousness. Musical instruments offer a vast array of the applications of various woods and reeds. The materials to record the thoughts and history of humanity and the many instruments used in various sports from skis to bats to goalposts are traditionally natural in origin, and the billions of tires on cars, trucks, and bicycles are derived in large part from the latex of the rubber tree, *Hevea brasiliensis* (Willd. ex A. Juss.) Müll. Arg. (Euphorbiaceae). Our past tells us how we have, over the millennia, already optimized thousands of well-characterized uses of plant, marine, and microbial systems. Our present is committed similarly. Our future will be even more highly dependent on optimizing and replenishing these natural resources as the finite fossil-based resources are depleted relentlessly. Maintaining access to those valuable resources in a truly sustainable and regenerative manner is the core future exploration for humanity, particularly for the natural product scientists pursuing the untrodden pathway towards maintaining the supply of medicines down which we are now engaged. Success along the pathway towards "complete sustainability" is no longer an option.

2. RESOURCE UTILIZATION AND OUTCOMES

The First Industrial Revolution is commonly considered to have started around 1760. Presently, the world is in the transition from the productivity-oriented Fourth Industrial Revolution (4IR) to the humanity- and eco-focused Fifth Industrial Revolution (5IR) [11,12]. That transition is proving to be extremely challenging and is being strongly resisted by the interested parties who continue to promote economic growth through the expanding utilization of non-renewable resources to a higher level of Gross Domestic Product (GDP), itself tied to the demands of a continuously increasing global population. Since those non-renewable resources of Earth are an aspect of the reasonably accessible planetary boundaries [13], that concept alone is an unsustainable pathway for Earth [14] and renders the term "Sustainable Development" an oxymoron [15,16].

"Sustainable Development" was originally proposed as an alternative to the zero-growth option [17]. It was always fundamentally anthropocentric towards continued economic growth through the increased GDP of a country and technological advancement, while not truly engaging sustainable environmental concerns in an ecocentric manner for the future [18]. Another approach to contemplate "sustainable development" is to ask, "How many and which of the 169 targets of the 2015 Sustainable Development Goals (SDGs) (*vide infra*) can be made "wholly sustainable" for generations to come?" This discussion will be continued when we examine what has happened recently to the timeframe of the SDGs, and their relationship to the term's "growth" and "degrowth" in evaluating sustainable natural resource needs for future generations. Where do those divergent pathways lead the planet and what does that mean for sustainable natural products in health care and other applications in future research and development?

The Fourth Industrial Revolution (4IR) and the Fifth Industrial Revolution (5IR) are fundamentally distinct through several perspectives [11,12]. The 4IR, which continues, is focused on the enhanced efficiency of processes, particularly integrating robotic elements and large data systems, while ignoring the human and environmental costs of optimizing production [11]. The concepts embodied in "sustainable development" were largely absent, and artificial intelligence, the internet of things, additive manufacturing, and cloud computing in industrial settings were the focus [11,12]. However, there is an element of sustainability towards enhancing value in products through integrated and resilient manufacturing, especially regarding the interrelationships of smart devices [19].

The evolution of the 5IR began in July 2020 through the European Commission, which focused on sustainability considerations and human interactions and was therefore more ecocentric [20,21]. The relationships with robots (now termed "cobots") are developed in terms of the capacity for synergistic and cooperative, not replacement, activities [11], in which human intentions and outcomes are critical inputs. In this scenario, robots learn tasks and implement them in a manner humans cannot possibly accomplish [11,12]. One example is for the synthesis of large numbers of organic compounds deploying an autonomous robot with a phalanx of reaction variables for a series of synthetic chemical processes with green chemistry optimization as the goal [22,23]. In addition to being ecocentric and having a sustainability dimension, 5IR also has the resilience quotient. That embraces exogenous factors for industry and academia, including continued access to requisite resources directly or through supply chains, the tracking of quality assessment systems through forms of blockchain technology, and resisting cyber-attacks, hacking, ransom requests, data manipulation, and data theft [24]. A more extensive discussion of 4IR and 5IR related to the future of natural products research is available [25].

The tension between the sustainability-related philosophies of 4IR and 5IR is evident in the industrial practices compared with the marketing of products. Widespread and deep shifts in the relationship of “development” to more equitable, human-centered practices and sustainable lifestyles which respect nature are needed [2,3,26]. The fundamental reality for urgent actions is being ignored, or in some instances being “greenwashed” at the global level [27]. Very well-known conglomerates are making substantially misleading, environmental or sustainability claims regarding their operations and actions, and the marketing of their products [28]. Meanwhile, the consumer/patient in society is calling for “real” lower carbon footprints with net zero goals by 2050 with a diminished focus on profit [29]. A 2020-2021 analysis of the on-line statements in the annual reports of the 20 major pharmaceutical companies regarding their environmental change targets, reductions in greenhouse gas emissions, and the strategies being implemented, revealed that only eight were striving for net zero emissions between 2025 and 2050 [30]. The moral, ethical, and practical environmental issues and implications reflected in this study for future generations are indeed profound and need to be addressed, especially as defossilization becomes more evident.

In retrospect, it could have been a very different scenario for 2025 and beyond. In July 1977, Dr. Frank Press, a geophysicist, and at the time President of the National Academy of Sciences, who served as a science advisor to four United States Presidents, wrote in a letter to then President Jimmy Carter, commenting on the “greenhouse effect” of atmospheric CO_2 over a 60-year timeframe “…. a climatic fluctuation of such rapidity could be catastrophic.” Warning in the letter: “the situation could grow out of control before alternate energy sources………… become effective.” He recommended that “…. we should emphasize ………solar electric, biomass conversion or other renewable energy sources.” Regrettably, he also stated: “The present state of knowledge does not justify emergency action to limit the consumption of fossil fuels in the near term.” [31]

For several years, *The Lancet* Countdown has examined the relationships between human health parameters and environmental change following the report of the 2015 *Lancet* Commission on Health and Climate Change [32]. That document concluded that anthropogenic climate change could undermine 50 years of public health advances, yet, if challenged comprehensively, was “the greatest global health opportunity of the 21st century.” The 2017 report, 25 years after the first UN Framework Convention on Climate Change (UNFCCC) meeting, bemoaned how many of the climate indicators, including carbon emissions and global air and ocean temperatures, rather being mitigated had steadily increased each year, “jeopardizing human life and livelihoods” [33].

In the mid-2020s, climatologists are unable to explain the pace at which global environmental changes are occurring [2,3]. The time is long past to change how humans show reverence and reluctance in utilizing the Earth’s remaining finite resources, oil, gas, and coal, in the next 25-30 years. Plans must be initiated for a more deeply considered role for the global use of (clean?) coal resources before 2100, when supplies will be exhausted. The opportunity cannot be squandered to control the access and optimize, in an eco-responsible manner, the utilization of these last remaining fossil-fueled assets. The still-discussed notion of the sustainable dissipation of finite resources, such as gas and oil [34], is an oxymoron. Only eliminating the use of gas and oil by 2040 and reducing the methane emitted by terrestrial, marine, and animal sources might begin to fulfil our profound moral obligations to our descendants, albeit leaving very limited, untapped fossil-fuel based resources for the remainder of human existence.

A more likely scenario, based on contemporary global corporate and government trends, and the overall modest financial commitments to alternative, renewable energy resources in many countries, is that since the financial tipping point targets for diverse investment strategies may have been passed, humanity is already on the pathway of essentially total gas and oil depletion by the mid-2050s. At which point, those assets are chimerical for all future generations. And then what happens? On this planet, with those few clearly defined non-renewable resources oil, gas, coal, and various precious rare metals, gone or not ecologically or economically accessible, the plan is to do what exactly?

From a patient perspective in the future, where and how does the consistent global provision of sustainable, safe and effective, quality medicines align in this scenario? Over the past 25 years there has been a series of huge, cutting-edge investments in drug-related, synthetic and natural product research infrastructure in China [35], as well as being the global leader in solar, wind, and electrical energy sources [36]. Based on the contemporary innovations [37], one can predict that by 2040, China will be the major global provider of medicinal and other biological agents from natural sources, poised for the transition to an all-natural, wholly sustainable supply chain in the 2050s.

For the future development of the remaining natural resources and their derived products, including medicinal, biological, and cosmetic agents, there are five factors which must coalesce to render a healthier Earth for the next generations: Sustainability, Environmental Change, Defossilization, Degrowth, and Money. These are no longer choices for humanity. The days of consciously ignoring the reality of living beyond the long-term carrying capacity of Earth, with high levels of pollution and environmental damage, and the mishandling of "waste", have long passed. In the process, many opportunities were, and are continuously, being missed. The challenge is, what is going to be the series of ameliorating actions humanity will now pursue? To date, they have been inadequate, as environmental deterioration continues at a pace. Overarching these factors, and an explanation of why the situation becomes more dire daily, is the failure of the most prolific planetary abusers and polluters to promote, not abrogate, global commitments of action and finance. Supporting, not deprecating, the promotion of sustainability, conservation, and restoration would embrace the economic, political, industrial, and conservation sectors for many environmental sites (and major cities!) in the world whose very survival is under continuous direct threat. As each Conference of the Parties (COP) meeting on either climate change or biodiversity passes without unequivocal commitments to strategic drastic actions and major financial support systems, the time frame shortens, the urgency grows, and the E.D.G.E. (*vide infra*) draws closer.

3. HOW DID WE GET HERE?

How did we get to this stunning place in the history of humanity? How is it possible that all the global and national meetings, conferences, pledges, agreements, etc., have utterly failed to produce a series of fully funded action outcomes to ensure the survival of humanity, and its development for a holistic, sustainable future? Governments and industries tied to their GDP are continuously promoting, still expanding, the extremes of fossil-fueled pollution and the exhaustion of non-replaceable assets, in part, by promoting population growth. The reality of ravaged and gutted resources and the inexorable environmental change is still being denied at the highest government levels. What is *their* plausible vision for humanity in 2050, 2060, and beyond for a global population of about 10 bn? Their silence regarding Earth's resource boundaries is breathtaking and should be deeply concerning for the rest of humanity.

There have been 29 Conferences of the Parties involving those 198 countries signatory to the United Nations Framework Convention on Climate Change (UNFCCC) which was finally adopted in 1992. For context, the first international conference on climate change (COP1) was held in Geneva, Switzerland in 1979. At COP28 held in Dubai in the United Arab Emirates in December 2023 the participants (finally!) agreed to be "transitioning away from fossil fuels with respect to energy systems." [38]. However, no benchmarks were identified, no timetable proposed for completing any defined targets, no strategies discussed and developed, and no pledges were made for the financing of such a dramatic transition to support the emerging world. Rather disturbingly, the well-established, dominant source of the climate deleterious gas, methane, namely grazing cattle and other ruminant animals [39], was not mentioned in the conclusions from COP28 [38].

The committed "transitioning" pathway from COP28 represents long-term global "defossilization", initially from the use of oil and gas as energy sources until exhaustion in the mid-2050s for all future generations [40,41]. Steadily declining accessibility to those resources will significantly impact human and planetary well-being from an energy perspective. Not discussed, is that those impacts will also pervade the chemical, pharmaceutical, and cosmetic industries (among others), well beyond the non-renewable energy production sector. It will represent a fundamental paradigm shift to maintain the feedstocks for the sourcing of chemicals for the processing and synthesis of many medicinal and biological agents, including natural products from marine, microbial, and plant-based resources. Corresponding compounds will be required through the development over the next 15-20 years of wholly sustainable, natural replacements. Anything less can only be a palliative, temporary response which ignores the generations beyond the 2050s. This challenging opportunity will evolve as an essential facet for the future research programs of natural product scientists and medicinal chemists for biological agents, and those scientists who are involved in optimizing drug delivery systems and the economics of accessibility.

Azerbaijan is planning to expand its gas production by 33% by 2033 to enhance their GDP [42]. COP29 was held in Baku, Azerbaijan with over 1,750 fossil-fuel supported lobbyists attending. There, funding for the COP28-approved "transitioning" process to aid emerging nations in moving away from fossil-fuel use for energy was a major discussion topic with a commitment for $350 bn/year by 2035. However, a major group of emerging nations at one point walked out of the sessions, and the culmination was that the meeting did not reach a consensus. The former UN Secretary General, Moon, Ban-Ki, the current UN Climate Chief, and many experts concluded that the meetings were moving too slowly and were "no longer fit for purpose" in addressing the urgent global issues (https://www.bbc.com/news/articles/cx2lknel1xpo). Massive global financial commitments, real funding, and strategic actions for the next 15-20 years are necessary to avert this looming ecological and economic catastrophe.

It should be emphasized that, at present, synthetic and semi-synthetic drugs require non-renewable resources for their generation, and natural medicinal agents require non-renewable resources for their processing from the original raw materials, be that a plant, a marine organism, or a microbial culture sourced either randomly or cultivated. When no processing beyond aqueous extraction is involved in making the medicinal plant product available for the patient, the long-term sustainability of individual plants in multi-component plant mixtures remains in high jeopardy. This is due to environmental modulations and over-harvesting which requires continuous monitoring if the plant material is being wild-crafted for consistent availability to be established.

A dedicated, strategic, prioritized, and sustainable response to continue modified access must be planned and developed in the immediate future to avoid significant gaps in the local and global medicines supply chain. Developing those approved, total replacement options for as many medicinal and cosmetic products as economically and scientifically possible from sustainable sources is a core activity within Medicines Security (*vide infra*). The critical issue is who will take leadership responsibility for these new, expensive, protracted, vital initiatives for the next 30 years at the international and local levels? One suggestion is for a dedicated "Medicines Security" unit within the WHO charged with coordinating medicinal agent replacement programs to avoid the unnecessary duplication of research and promote cooperation between countries to address these scientific challenges. Certainly, a major international conference should be developed as a matter of urgency that would identify the scientific and technological gaps to be filled and the industrial nations with the capacity to address these issues for global and local populations.

Over the past five years, one of the most vocal global leaders for changing fossil-fuel based energy habits has been the UN Secretary General António Guterres. He has been very forthright in his warnings concerning the impending situation. In 2021, at the COP26 meeting in Glasgow he stated that "…we remain on track for a catastrophic temperature rise well above 2 degrees Celsius." After the release of the Intergovernmental Panel on

Climate Change (IPCC) report in April 2022, he indicated that "New fossil fuel investment is moral and economic madness". At the Davos Economic Meeting in January 2023, he shared that "Today, fossil fuel producers and their enablers are still racing to expand production, knowing full well that their business model is inconsistent with human survival. This insanity belongs in science fiction, yet we know the ecosystem meltdown is a cold, hard scientific fact." At the United Nations Climate Change Conference (COP28) held in Dubai in 2023 he commented that "We are living through climate collapse in real time". In June 2024 he urged ".... every country to ban advertising from fossil fuel companies, and every news media and tech company to stop taking fossil fuel advertising." Finally, at the Davos Meeting in January 2025, his comments became even more pointed. "A number of financial institutions and industries are backtracking on climate commitments…. I want to say loudly and clearly: it is selfish and also self-defeating. You are on the wrong side of history. You are on the wrong side of science." At the United Nations General Assembly meeting in New York in September 2025 his comment was "Fossil fuels are a losing bet".

3.1 The Paris Agreement – Dead or alive?

At COP22 held in Marrakesh, Morocco in 2015, the legally binding Paris Agreement was signed by 196 countries. They concurred with respect to modifying energy practices to keep the global air temperature increase below 2.0ºC, or preferably 1.5ºC, compared with pre-industrial levels, and to report their progress. It was estimated that such a target would necessitate a 50% reduction in global fossil fuel emissions by 2030. Countries were encouraged to develop their own plans for achieving that target. However, the Nationally Determined Commitments (NDCs) are not legally binding due to arduous lobbying efforts which have also infiltrated the political domain in terms of freezing local actions towards the targets, such as reducing or eliminating the sale of fossil-fuel using vehicles by a specified time. Although a signatory to the Paris Agreement in September 2016, the United States formally withdrew as a signatory in November, 2020. It re-signed in January, 2021, and then withdrew again in January, 2025 under divergently committed political parties. The only other non-signatory countries to the Paris Agreement in January, 2025 were Iran, Libya, and Yemen. As a prelude to the Paris Agreement, the US has not ratified the Kyoto protocol from COP3 in 1997, nor has it ratified the Rio Convention on Biological Diversity (CBD) from 1992. Interestingly, only three other countries, Andorra, South Sudan, and the Holy See have also not ratified the CBD.

The average global air temperature for 2023 and for 2024 reached the limit of 1.5ºC recommended in the Paris Agreement of COP22. As each month sees warmer average global temperatures, the long-term 1.5ºC increment over preindustrial levels is now regarded as being an impossible target [43,44]. Under these potentially disastrous circumstances alternative pathway solutions are clearly needed [45] and some approaches will be mentioned subsequently. Which brings us to "time".

Time is now *the* pertinent and overarching enemy to forestall the obvious environmental trends and avert the catastrophic, domino-style, collapse of multiple global systems in the mid-2050s or sooner [2]. Endless talking and continuous obfuscating are not a solution for the survival of humanity. Inadequate financial commitments to addressing climate change over massive energy sector profits are deeply immoral with respect to the countries of the South, who have contributed very little to the negative environmental changes to which they are being subjected, and to the welfare of their descendants. Only profound, urgent, positive actions and substantive behavioral changes in fossil-fuel derived emissions, predominantly by the countries of the North, can be deemed relevant at this decisive anthropogenic junction. In a statement following publication of the UNEP Emissions Gap Report in October 2024 [46], the U.N. Secretary-General, António Guterres made this dire situation abundantly clear: "We're playing with fire; there can be no more playing for TIME. We're out of TIME. Closing the emissions gap means closing the ambition gap, the implementation gap, and the finance gap. Starting at COP29."

At COP15, the 15th Conference of Parties to the Convention on Biological Diversity held in December 2022 in Montreal, Quebec, Canada, 23 global targets were established for 2030 and became part of the Kunming-Montreal Global Biodiversity Framework. Among them were, a short-term goal for conservation funding of $20 bn in 2025. The conservation aims were to protect 30% of terrestrial and marine environments, to restore 30% of degraded ecosystems, to reduce pollution from all sources, to reduce the impact of climate change and ocean warming and acidification, to halve food waste, and to require the monitoring by transnational companies and financial institutions of their biodiversity impact.

At COP16, held in Cali, Colombia in October-November, 2024, seven of the richest countries pledged $163 million toward the Global Biodiversity Framework Fund. Twenty African Countries demanded that those seven countries "urgently deliver new international funding for biodiversity." The conclusion was that funding for global biodiversity initiatives is going nowhere, and the conference was placed in suspension until late February 2025 in Rome. The meeting then adopted the Monitoring Framework for the Kunming-Montreal Global Biodiversity Framework and Resource mobilization and focused on enhancing investments for biodiversity conservation and ecosystem restoration. Developed countries pledged $20 billion annually for 2025 and $30 billion by 2030. Although at the time of the meeting only $383 million was actually committed. Businesses relying on biodiversity were also asked to contribute to the “Cali Fund”. Reporting frameworks and progress indicators were recommended for restoration with a goal for at least 30% of degraded land, marine, and freshwater systems to be restored by 2030, which supports the UN Decade of Ecosystem Restoration program for 2021-2030 [47].

3.2 The changing world in 2025

In November 2025, the global population was 8.255 million and is scheduled to reach 9.85 million in ca. 2057 [48], by which time the supplies of natural gas and oil are projected to have been dissipated or be at a very low level and thus available only at very high cost [41,42]. Glaciers are disappearing at an alarming rate in the high mountains of the world [49,50] and in the Arctic and Antarctic regions [51]. There is deep concern about the rapid demise of the Thwaites Glacier (the “Doomsday Glacier”) in West Antarctica [52]. That glacier is the size of Great Britain and is melting from the warming of the ocean rather than the warming air. It is estimated that global sea levels would steadily be raised worldwide up to 6 ft by 2100 if the glacier continues to melt and is eventually lost [53]. Because it blocks the melting of other ice formations in the West Antarctica, sea levels could increase by 10 ft globally if more glaciers succumb to melting.

Major cities around the world, including Bangkok, Jakarta, Manila, Miami, Mumbai, New York, and Venice are already threatened with being permanently flooded in the next 15 years without drastic local action [54]. A global analysis of 293 port cities using a system for predicting local sea level change and the primary causative source was applied to identify additional susceptible areas of concern [55]. As a result, many other cities in Europe and Asia are now regarded as highly vulnerable, including London, Amsterdam, Hamburg, Shenzhen, and Dubai [56]. In response to the flooding and sinking situation in Jakarta, Indonesia is moving its capital to Nusantara, East Kalimantan on the island of Borneo over the next 20 years [57]. Low-lying islands, particularly many western Pacific nations, are under serious threat of disappearing completely [58]. Nations with many small island communities, including Indonesia (ca. 6,000 islands), the Philippines (ca. 2,000), Sweden (ca. 1,000), Finland (ca. 1,000), and Norway (ca. 1,000) will be forced to introduce existential migratory activities to preserve the integrity of their populations [59]. The New York City area is expected to lose 80,000 homes to persistent flooding by 2040 [60] and the English coast will lose up to 160,000 homes by 2050 [61].

The projected increases in sea levels will undoubtedly affect the salinity of all coastal areas where medicinal, culinary, and cosmetic plants are being cultivated and harvested. How the change in salinity will the growth and metabolite profiles of these individual plants remains an open question for investigation, with some preliminary results reviewed [62-64]. Studies have been reported for several culinary medicinal plants, including *Ocimum* spp. [65], safflower [*Carthamus tinctorius* L. (Asteraceae)] [66], and *Thymus* spp. [67]. Extensive, more definitive, local studies will be needed as the salinity of the soil becomes increasingly impactful to assess changes in biomass, metabolite profiles and production levels, and the resulting biological effects for commercial species. Consistency is a fundamental attribute factor in all aspects of plant cultivation, whether for foodstuffs or biological agents [68,69].

A pertinent and urgent question for the future of agricultural, medicinal, culinary, and cosmetic crops, as environmental change proliferates, and as the demand for cultivation increases, will likely become "Where *can* we grow our crops in a consistent and reproducible manner?" Melting of the Himalayan glaciers has provided water for agriculture and social uses for many countries in South and Southeast Asia for thousands of years. When global warming reaches 3ºC, and the glaciers are not being replaced through new snowpacks, the food and medicinal plant sources of hundreds of millions of people will be threatened [70]. Drought in southern Europe and Mesopotamia, and in the southern United States, could reduce agriculture opportunities even further, as the IPCC has warned [71]. These potential changes in access to food supply are likely to produce mass migrations and/or civil unrest, as has been seen in Somalia [72] and Guatemala [73].

Beyond rising sea levels, salinity concerns, and receding glaciers are considerations for the metabolite profiles and plant damage which occurs under highly variable weather conditions, and which will induce unpredictable changes in the biological consistency of the crop [71,74-78]. A report presenting the significant role of global warming in eliciting extreme weather events in North America, Europe, and many parts of Asia in the period 2016-2024 is available (https://interactive.carbonbrief.org/attribution-studies/index.html). Twenty-four "impossible heatwaves" and 550 heatwaves, floods, droughts, and wildfires were identified as more intense or more frequent in the timeframe. In contrast, extreme snow and intense cold events were reduced. These unexpected weather outcomes alone were reported to be responsible for 100,000 premature deaths per year.

In March 2025 the UN World Meteorological Office issued a *State of the Climate 2024* report [79]. The report established that 2023 was the hottest ever in the 175 years of recording data. The average global temperature exceeded the 1.5ºC recommended in the Paris Agreement, and ocean temperatures have increased every year for the past eight years. Glacier loss in the period 2021-2024 was the greatest recorded, resulting in doubling of the rate of sea level rise to 4.7 mm/year in the period 2015 to 2024. Carbon dioxide, methane, and nitrous oxide levels are at their highest levels in the past 800,000 years [79]. What are the eco-facts needed to convince world authorities and governments to act? For the fossil-fuel companies to stop their aversion to change for the sake of humanity? What more evidence is needed as the global situation worsens month by month?

It must be noted that there is a fundamental, perhaps fatal, certainly unappreciated flaw in the Paris Agreement recommended limits of 1.5ºC or worse 2.0ºC by 2050. It is this. Earth is not like an oven where, once a certain temperature is reached, the temperature can be stabilized for cooking, or the heat source can be turned off for cooling. For Earth and the continuing energy and fossil-fuel based resources still being utilized after the 1.5ºC threshold is surpassed permanently, the heating effects won't stop suddenly. They will continue for an unknown period with further unpredictable results. Even utilizing renewable sources (wind, solar, etc.), heating associated with numerous human activities will still be occurring. Earth will remain in a prolonged state of excessive heat, with no apparent recourse [80]. Which begs an important question. Did Earth already pass a critical tipping point of global air temperature in 2023 (and probably 2024) and no-one has realized or said anything?

Recognizing that Earth's fossil-based and rare metal resources have boundaries of availability [81], modulations in local human populations are a mitigating factor in establishing timeframes for resource depletion, particularly based on land use profiles. Projected national population increases and decreases between 2025 and 2050 vary widely, with the population of Japan projected to decrease by 14.9% and China by 11.1%, as the population of Pakistan rises by 46% to become the 4th largest in the world, and Nigeria increases by 53%, Ethiopia by 68.5%, and the Democratic Republic of the Congo by 99.6% by 2050 [48]. Several countries with declining populations, including China, Japan, Korea, Taiwan, Singapore, Russia, Denmark, Greece, Italy, United States, and Germany are actively promoting procreation (a.k.a., pronatalism) on economic grounds, and providing financial and other incentives for "success" [82]; an irredeemable approach to fostering a sustainable Earth for future generations.

Through interconnectedness, including fascinating trophic relationships of direct dependence [83], the loss of one species of animal, plant, marine organism, or insect may result in the loss of other species [8,84]. Terrestrial biodiversity losses of flora and fauna are staggering, with over 10,000 acres lost/day in the Amazon region alone [85]. The number of plant species disappearing each year is unknown, as at present there is no well-established system for tracking species globally. Four factors, including timber harvesting, edge effects, fire, and drought have also been exacerbated through anthropogenic activity, and will remain threats to global biodiversity for the next 25 years [86]. Over-utilization of arable land has led to an erosion in the quality of the soil, with no natural source of replenishment, resulting in a reduction of crop yields [71]. From a food perspective, the dramatic decline in fish stocks [87,88] due to overfishing and the deep trawling of the seabed, and the damage to coral reefs [89,90] has resulted in major concerns regarding the short- and long-term supply of dietary fish and is threatening marine bioprospecting. A report from October 2025 concluded that the bleaching of the coral reefs is now beyond their tipping point, jeopardizing all the parts of the web of life which rely on the viability of coral reefs [91]. Since 90% of global warming is absorbed by the oceans [92], there is an ongoing lowering in the pH (acidification) from CO_2 which impacts the feedstocks of marine organisms [93], including the fish that are predated. That is leading to the disappearance of other marine animals of potential interest for their (or their symbionts') bioactive metabolites [94]. Are we witnessing the sixth mass extinction in the history of Earth [95], and the first due to deleterious anthropogenic activities? A United Nations group, The Intergovernmental Science-Policy Platform on Biodiversity and Ecosystem Services (IPBES), based on 15,000 studies, first reported on the unprecedented and accelerating rate of biodiversity loss in 2019. A draft of a second report was discussed in June, 2024 (https://www.biodiversa.eu/2024/06/11/webinar-review-the-ipbes-second-global-assessment-draft-scoping-report/), and remains to be approved and released. Biodiversity loss has been described as a "biological annihilation" for which "humanity will eventually pay a very high price" [96].

In its latest summary of the *State of the Worlds Plants and Fungi, 2023* the Royal Botanic Gardens at Kew indicated that global herbarium records embrace 350,386 vascular plants in 642 families, of which 28,187 plants were reported to have various medicinal uses [97]. However, that is historical information not contemporaneously sourced. It is unknown how many of those species remain in existence, where they are to be found, or how many are in contemporary use and therefore important for conservation and sustainability efforts. More importantly, there seems to be no plan to establish where the key global medicinal plants are located and investigated as a prioritized, essential aspect of the sustainable sourcing component of Medicines Security (*vide infra*) [25,98,99]. Initiatives to fill these highly significant knowledge gaps should be initiated by WHO as a part of the expansion of their programs in traditional medicine [25].

Of significance is what the anticipated global and local roles of the large and smaller botanic gardens around the world should be to establish where the most important medicinal plants are, their contemporary status. Who within a country or region is collecting and collating that information for the systematic tracking of potential resource needs [25]? In terms of medicinal plant applications, it was guesstimated by an expert panel at WHO in 1985 that about 74% of the global population in emerging economies uses medicinal plants as a primary source of healthcare [100]. In Jamaica, a rare local study of the functional role of medicinal plants in primary health care, bore out this level of usage [101]. As the most significant expansions in population within the next 25 years will occur in many of the countries in the lower emerging economic groups in the world, what does that mean in terms of the sustainability, standardization, and utilization of medicinal plant resources for prioritization in patient care, as well as for other purposes?

4. SUSTAINABILITY AND SUSTAINABLE DEVELOPMENT

Maintaining the supplies of food, medicines, and cosmetics derived from natural resources has been a concern for humans since they settled in communities around 12,000 years ago. The Greek philosopher Plato (5thC BC) and centuries later, the Roman natural philosopher, Pliny the Elder (1stC AD), expressed concerns for environmental degradation from human activities, such as farming, logging, and mining [15]. The term 'sustainability' was first used by a mining manager, Hans Carl von Carlowitz, in the book *Sylvicultura Oeconomica* in 1713. Carlowitz proposed the "nachhaltende Nutzung" (sustainable use) of forest resources to maintain a balance between harvesting old trees and planting trees for the future.

It was over 270 years before the pioneering 318-page Brundtland Report *Our Common Future* was presented in 1987 [102,103]. It brought global prominence to a contemporary concept of sustainability and indicated that the environmental concerns were beyond local and that consequently a global response was required, and not one reflective of nationalistic and/or business self-interests. It called for efforts "to deal successfully with protecting and enhancing the environment, a long-term agenda for action during the following decades… (*to fulfil*) …the aspirational goals of the world community." Importantly, it was quite holistic in approach through addressing population and human resources, food security, biodiversity and ecosystems, industry, energy, and the depleted environment. However, concerns regarding the availability of synthetic and natural medicines and cosmetics were not raised.

Rachel Carsons' *Silent Spring*, published in 1962 [7], which led to the banning of the insecticide DDT in many countries, had drawn, in clear terms, the correlation between continuous economic growth (i.e., a GDP) and degradation of the environment, notably through the loss of biodiversity. Ten years later, that interrelationship was developed further within a simulation model published in 1972 as *Limits to Growth* under the aegis of the Club of Rome [104]. Population growth, agricultural production, the depletion of non-renewable resources, industrial output, and increasing pollution levels were the key factors modeled to examine what continuous economic expansion and population growth could mean for the planet. The two main conclusions were that in the absence of a change in the growth systems the planetary boundaries would be reached within 100 years (i.e., by 2072) resulting in an uncontrollable decline in population and industrial production. Countering with: "The challenge of overshoot from decision delay is real, but easily solvable if human society decided to act" resulting in ecological and economic stability into a future "capable of satisfying the basic material requirements" of the projected global population [104]. Those conclusions were presented when the population stood at only 3.845 billion. In the past 53 years there have been several updates assessing *Limits to Growth*. Almost all have concluded that the developed models were quite accurate from a tracking perspective although they should not be used as a predictive tool [105-108]. In part this is because a contemporary, overarching, mitigating factor that was not originally included in the modeling processes are the ongoing and dramatic climate changes being witnessed globally in the past 50 years, and the resulting environmental and sociological impacts of those changes locally and regionally.

In 1980 the International Union for the Conservation of Nature (IUCN) provided an early reference to the concept of "sustainable development" as a priority for the world [109]. Subsequently, the Earth Summit held in Rio de Janeiro, Brazil in 1992, which resulted in the development of the Convention on Biological Diversity (CBD), extended the focus on sustainability, which eventually led to the evolution of the Millennium Development Goals for 2000-2015 [110], followed by the vastly expanded Sustainable Development Goals for the period 2015-2030 [111].

At the millennium, new global directions for the United Nations were sought, and following the Millennium Summit, eight Millennium Development Goals (MDGs) for 2000-2015 were agreed to by the 191 UN member states [110]. Each goal had several targets, resulting in 21 targets overall. In 2004, the fundamental question of whether the MDGs could be achieved was posed [110] and analyzed regarding the troubling issues of limited funding, limited applicable metrics, and the legitimacy of the North driving the processes with only modest input from the South [112]. The absence of a clear emphasis on environmental sustainability was also of concern. The United Nations *2030 Agenda for Sustainable Development* expanded the eight MDGs to seventeen Sustainable Development Goals (SDGs) with 169 targets and some selected indicators [111]. A definitive treatise on the developments of the concept and providing some of the metrics and pathways as an adjunct to the Sustainable Development Goals (SDGs) was presented by Sachs in 2015 [113], who had been intimately involved with the promotion of the original MDGs.

The terms sustainability and sustainable development are sometimes confused. In 2015, UNESCO made the distinction as the former being a long-term goal for humanity, whereas the latter refers to the processes to achieve the goal [114]. Sustainable development therefore envisages a society where human needs for living and the requisite resources are utilized with integrity [115,116] and do not imperil Earth's resources for future generations. Yet even a cursory review of the long-standing issues and the deeper contemporary concerns in the SDGs reflect the limited progress made during the past 45 years.

It is generally considered that "sustainability" is founded on environmental, economic, and social aspects [117] enabling current and future generations to live harmoniously on Earth. Several definitions of sustainable development are available [15,102,110,115,116,118,119], but possibly, like the many definitions of an "alkaloid", it matters not [120]. Awareness and understanding of the concepts and issues and collective and collaborative actions are what does now and will forever matter.

Clarifying, the term "Sustainable Development", as formulated, is widely considered to be an oxymoron [15,16], since in the current understanding the term "development" itself implies economic expansion at the national level and the continuous linear (access, production, use, disposal) utilization of non-renewable resources. Without fundamental philosophical reassessment of the ongoing pathway, the concept only achieves reality when framed as the "development of sustainability". After all, any development goal which depletes Earth's resources without dedicated and assured compensatory replacement or regeneration, also becomes an anathema for the future generations.

The search by humanity for "Sustainability" can only have a single, simple "goal" for completely non-depleting integrity for all human activities on Earth. In reality, it is the forever journey for a steadily increasing population scheduled to reach 10 billion in 2060 and about 10.2 billion by 2100 [48]. As this practical and morally transformational journey unfolds, what is the plan for the development of global resources in a wholly sustainable manner to provide the needs for a steady state global population of 9.0 or possibly 9.5 billion? A UNEP Resource Panel in 2011 recommended that the alternative pathway is to disengage economic growth from the consumption of natural resources [121]. That would involve decoupling from the excessive exploitation of natural resources and the extensive levels of waste and other residues of processing which lead to negative environmental impacts and a widening gap in socioeconomic standing.

As the demand for more raw materials increases, including for pharmaceuticals, traditional medicines, culinary plants, and essential oils, how can these essential components of integrated healthcare and commodity systems be made sustainable and interface with other societal parameters locally and globally in the diverse economies?

A linear model will clearly not achieve that goal as it continues the very high levels of final product disposal. One suggestion is that only a "circular value ecosystem" based on the transitioning of waste, various residues, and obsolete products into assets of value can aid in regenerating capital for individual emerging economies [122]. The more complete utilization of natural and manufactured products, and some aspects of creating a (bio)circular economy for resource sustainability, coupled with the future, essential role of diverse natural products in those processes, are discussed subsequently.

If, as some would claim, sustainability is a goal, then what lies beyond sustainability? Regeneration? Replenishment? Or is it the inexorable, discombobulating collapse of the environmental, social, and economic parameters, perhaps over decades or possibly a few hundred years? Sustainability is now similar in some respects to a never-ending train journey, where one is always looking out of the window to check the everchanging landscape. Aggressive, continuous monitoring by the respective local and global agencies will be essential. One of the outcomes of COP16 envisaged for biodiversity and environmental restoration is to provide the resources "lost" through transitioning from fossil fuels (COP28). Along the way, monitoring will also be essential for tracking the substantial annual financing and other material resources required for that transitioning process (COP29).

The significant difference is that, unlike the archetypal train journey on a pre-constructed track through valleys and dark tunnels and up mountainsides, Gaia is on a journey, like the eponymous starship "Enterprise", where it has never gone before; except we cannot leave Gaia. There can be no taking "the road less travelled" as the poet Robert Frost iconically recommended in *A Road Not Taken* in 1915. It is the present and coming generations who are now responsible for creating and pursuing that one-way passage of time, oblivious and naïve of where it will lead planet Earth, and how long the "ride" will be. We are in the uncomfortable position of "hoping for the best". A phrase first annunciated by Cicero in 46 BC. While the caveat, "and planning for the worst", originated with the late creative writer and artist Maya Angelou. Developing plans requires initiation, intention, and creativity for any possible actions of implementation to follow. Who will initiate the plans for beyond 2050?

4.1 Sustainable Development Goals – Shifting the goalposts to 2050

In Re-iterating, the UN Sustainable Development Goals (SDGs) for the period 2015-2030 are comprised of 17 goals and 169 targets within those goals [123]. Depending on a personal viewpoint, nine of those goals could be impacted by various perspectives of the development of natural products and medicinal agents in society: Zero Hunger (SDG 2), Good Health and Well-being (SDG 3), Quality Education (SDG 4), Sustainable Cities (SDG 11), Responsible Consumption and Production (SDG 12), Climate Action (SDG 13), Life Below Water (SDG 14), Life on Land (SDG 15), and Partnerships for the Goals (SDG 17).

However, a summary of the status of the SDGs in September, 2024 indicated that *none* of the 17 goals would be achieved by 2030. Indeed, it was estimated that only 12% of the 169 targets would be achieved within that timeframe [124]. One example presented was that 2.2 billion people (~26%) on the planet still lacked access to safe drinking water. Two of the reasons presented for the anticipated failure after 10 years of global effort were that methodologies and standards were still lacking for 40% of the targets (e.g., for SDG 13), and that one-third of the countries were not generating and sharing the data on their progress.

A detailed critique of the status of the SDGs [125] pointed out in responding that they were not necessarily aligning their SDG goals. For example, they were supporting carbon-intensive industries while ignoring the impact of those activities on health care, employment, poverty, and the environment, and not encouraging investment in renewable sourcing. The group identified six priority areas requiring attention to improve responsiveness to the SDGs: i) extend and bolster the framework; ii) ensure a healthy planet; iii) enhance planning and cooperation; iv) address investment and finance; v) adopt mission-based approaches; and vi) foster change and accountability. For the nine selected SDGs, namely #1, 2, 4, 6, 7, 11, 13, 14, and 15, a global action timetable was suggested for 2030, 2040, and 2050, and a set of cohesive targets for 2050, focused again on net-zero carbon emissions, was proposed [125].

It was suggested that a revised and re-energized SDG framework be adopted, incorporating the ambitious goals for 2050 that would align with other global targets, such as the Paris Agreement. It was also recommended that high-income countries re-examine the global financial structure for implementing the SDGs and provide strong support for low- and middle-income countries to participate fully, achieve change, and develop a governance mechanism that could monitor the risks and potential outcomes of exceeding planetary boundaries [125]. These admonitions and new concepts formed the basis for the UN to re-examine the pathway beyond 2030 for the SDGs by setting a new series of initiatives for 2050.

The “UN Summit of the Future” held in New York in September 2024 developed three documents, the most important of which is the wide-ranging *Pact for the Future* [126]. Six major initiatives for 2050 were proposed, and within “Sustainable Development and Climate Action” one of four actionable commitments was to rethink what “progress” means for humanity and what “development” metrics are needed that go beyond the widely employed GDP metric. It was recognized as important to assess the well-being of humanity and the planet; a topic that is discussed subsequently. Within “Science, Technology and Innovation and Digital Cooperation” were suggestions to i) “scale up the means of implementation to developing countries to strengthen their science, technology and innovation capacities”, ii) “ensure that science, technology and innovation contribute to the full enjoyment of human rights by all”, iii) “protect, build on and complement indigenous, traditional and local knowledge”, and iv) “strengthen the role of the United Nations in supporting international cooperation in science, technology and innovation” [126]. The future opportunities for pharmaceutical research in general are clearly delineated therein, in which, as in the macrosystem, technology evolves as interdependent and integrated with the natural system. An essential requirement for serving the needs and development of the component sectors of Earth sustainably is embraced within the integrated research concepts for initiatives based on “cyberecoethnopharmacolomics” [98,99,127].

Another of the six major initiatives from the 2024 UN Summit is in Action 10 of “Sustainable Development and Financing for Development”, which includes the statement. “We must conserve, restore and sustainably use our planet’s ecosystems and natural resources to support the health and well-being of present and future use and restore seas and freshwater resources, and the forests, mountains, glaciers and drylands, and protect, conserve, and preserve biodiversity, ecosystems and wildlife” [126]. No mention is made regarding the relationship to health care needs for maintaining medicines, and the need to create a financially supported sustainable research and industrial environment where those basic human needs for prophylaxis and healing during the “transitioning” period to 2050 are researched appropriately from renewable resources, assured for patients, and the sourcing protected for future generations. However, these considerations clearly define the areas of research for the pharmaceutical and natural product sciences for the next 25 years. Despite these omissions, it should be recalled that health is a fundamental human right as indicated in Article 25 of the *Universal Declaration of Human Rights* from December, 1948.

Sustainability is, and will continue to be, a very, very difficult journey for humanity. It requires dedication, in many diverse situations, to paradigm-level changes in thinking, daily behaviors, and pursuits, beginning with a universally accepted recognition that the challenge is now, and that the reality must be pursued aggressively. Several barriers to sustainability have been identified [128,129], including intrinsic barriers that relate to the natural interdependency of everything on Earth [130] and that philosophical convictions do not automatically result in subsequent actions [131]. Other barriers are extrinsic in nature and thus, in principle, may be overcome.

There is the constant tension between environmental policy objectives, which typically lack incentives, and policies that directly promote growth (i.e., an enhanced GDP), expressed in terms of economic development and societal wealth [129]. Issues related to what and how we produce, consume, and dispose of materials, the linear economy [131], particularly in highly competitive, low profit markets, also limit the implementation of societal patterns of change [132]. That may appear as the conflict of short-term profit versus longer-term viability and can become a political response issue where the financial outcomes are timed in months rather than years or decades, and is characteristic of a linear, rapid response, outcome-focused, economy [131]. A report from the World Business Council for Sustainable Development assures in their *Vision 2050 – Time to Transform* document "a world in which 9+ billion people can live well, within planetary boundaries by 2050" [133]. They envisage restoring damaged ecosystems, reducing polluting emissions, and promoting sustainable agriculture [133]. However, there remains the unaddressed paradoxical thinking of the sustainable use of non-renewable resources which have finite boundaries. Can sensitization to the value of natural resources and how they are used be changed to promote meaningful actions at the government level? Each country will inevitably be obliged to face that challenge.

Many people, particularly in the developed world, the "North", have a significantly diminished awareness of their moment-to-moment relationship with nature. For the majority in the world, however, nature is a prescient issue and on-going, day-to-day concern. The list of "contact points" between humanity and the biologically important metabolites of nature is extensive [8]. Most of those applications will continue to require natural resources for many years ahead. How that can be achieved is a principal facet of the journey for humanity with sustainability as the criteria.

Human history shows how we reached this potential inflection point in terms of development, and what experiences led to the optimal use of selected plants as an interdependent support system for the presently varied global lifestyles. These lifestyles are essentially and inextricably deeply tied to plant-based resources; even more than St. Hildegard could have ever imagined. More critically, the future, particularly relating to biologically active natural products and the closely related semi-synthetic medicinal agents, will depend, to an ever-increasing extent, on the judicious and fully optimized use of sustainable plants and other natural resources to meet the expanding societal needs. These resources are vital for engaging in the concept of well-being, for humans, and directly and indirectly through trophic relationships, to maintain the operational web of life, Gaia, for the healthy survival of the organisms of Earth. Those considerations lead to the importance of Medicines Security, and the origins of sustainable, ecologically supportive, biologically active agents for future patients and animals needing prophylaxis or medical attention and care, and for the development of ecofriendly biocides.

5. THE PATHWAY TO MEDICINES SECURITY

One can turn the iconic thoughts of St. Hildegard of Bingen [5] around in two ways. Firstly, we can ask, can humanity survive on Earth beyond the resource boundaries? Secondly, how can we parse the boundaries of Earth's resources if we don't know what they are, where they are, what, on a prioritized basis, needs to be and can be sustained, and what can (and cannot!) be regenerated? Sustainability, this stunning, profoundly challenging, dangerous if we fail, forever journey of humanity, must now be the first consideration in any scientific initiative related to ethical societal development [26]. This is especially the case for future natural products and synthetic chemistry initiatives, including those for new or replacement medications, since if they are successful, they will have to endure. Two requisites for harmonious human survival on a global basis, beyond shelter, clothing, and safe water, are access to healthy food [26], to which we must now add access to safe, effective, consistent, and available medicines [98]. Stunningly, at the present time, only one of those requisites, food, is consciously secured globally through a responsible United Nations agency.

On October 16, 1945 the Food and Agriculture Organization (FAO) was founded in Quebec City, Canada. The stated goals were to achieve global food security, alleviate hunger, promote improved agricultural practices, and enhance nutritional outcomes. Now based in Rome, Italy, it currently operates in over 130 countries as a specialized agency of the United Nations. The World Health Organization was founded on April 7, 1948 as a United Nations agency aimed at setting international health standards, coordinating public health improvements globally, and responding to global health challenges. The WHO Constitution focuses on overall "health", mentioning "pharmaceutical" products in "international commerce" and their standards only in Articles 2 and 21 [134]. In the latter Article, WHO assigned itself the roles of adopting regulations for "standards with respect to the safety, purity and potency of biological, pharmaceutical and similar products" and for the "advertising and labelling of biological, pharmaceutical and similar products". Neither of these functions appear to have been initiated at the global level, with each country acting quite independently from a regulatory perspective, albeit based on WHO recommendations in some areas of practice. The continuing lack of regional standards for traditional medicines, other than for levels of heavy metals (Hg, Pb, Cd, and As) does not enhance healthcare, improve the commercial distribution of safe and effective products for manufacturers, or improve product safety, efficacy, consistency, and availability for the patient [25].

Consequently, unlike the mission of the FAO in an era of climate modulation where the impacts on commercial food supplies have been studied and acted upon continuously over many years [135-138], maintaining availability and supply chains for any form of synthetic or natural medicine is not indicated as an activity within the WHO Constitution, or an activity that has been acquired. This omission has become an exceptionally glaring, almost inexplicable, oversight. Possibly, the two prevalent myths of medicinal agents were (and are!) operating: that "the plants will always be there", and that "the chemicals for pharmaceutical and biocide synthesis will always be there". Contemporary experience indicates that these assumptions are very seriously misplaced. The concept of "Medicines Security", and of putting considerations for patient needs first, initially grew out of that omission as a major role for WHO. The implications for the future of global health as non-renewable resources are dissipated and as the environmental conditions and supply systems are modulated for natural and synthetic medicinal agents are abundantly apparent [98]. Indeed. they beg the global question of "Who's going to be in charge?"

As indicated, despite their practical dominance in global healthcare, especially for seven of the eight most populous countries in the world, which represent 46% of the global population, traditional medicine systems and their associated indigenous knowledge systems were not included in the WHO Constitution. In fact, the terms "traditional", "indigenous", "natural", and "plant" are not mentioned at all. It was only in 2002 that acknowledgement was granted, when the first *WHO Traditional Medicine Strategy 2002-2005* was published [139], with the most recent version prepared for the period 2014-2023 [140], and with a draft document available for review for the period 2025-2034 [141] for presentation at the 78th General Assembly of WHO in May, 2025. The first International Congress on Traditional Medicine was held in Beijing in November, 2008, where the "Beijing Declaration" was announced [142]. Member states were asked to develop policies which would ensure that traditional medicines were safe and effective, to develop licensing programs for practitioners, and to encourage communications between health care systems which would foster their integration. A recent article [25] has indicated how WHO should be significantly more active in promoting forty areas for traditional medicines to improve global health care for patient benefit. These initiatives include the fundamental scientific attributes embedded in Q.S.E.C.A., harmonization of regulatory control, personnel training programs, and integration into national health care systems. As a patient, these attributes are collectively and individually important in assuring that the medicines being presented to the patient in whatever form are indeed fully authentic and not fraudulent, for which WHO has indicated their concern [143].

5.1 The resource needs

It is axiomatic that a Healthy People require a Healthy Earth. Humanity is intrinsically inseparable from the basic requirements of vibrant, productive, and economically stable communities. If the world needed convincing, the pandemic of SARS-Covid-19 provided a tragically vivid illustration of the reality of the concept as economic and medical systems came near to collapse, even in highly developed countries, for an extended period. Global deaths from SARS-Covid-19 since its inception to late-2025 are about 7.09 million, corresponding to ~1% mortality rate. A toxic Earth, through polluted air, soil, and water, floods, fires, and drought, in addition to variable disease prevalence, causes massive, rapid, economic tragedies, and unprecedented changes in lifestyle, and deleterious health consequences [144]. We must be especially wary of the contemporary toxicities which result from the anthropogenic impacts of the global warming of the air, of the earth itself, and of the oceans. Some of these may include, as extreme weather events become more prevalent, increases in asthma and cardiovascular disease, and changes in vector ecology leading to an increased incidence of malaria, dengue fever, encephalitis, West Nile virus, and chikungunya, and their appearance in new cluster areas. Rising sea levels could lead to enhanced deleterious health effects from polluted water, such as cholera, leptospirosis, and more widespread toxic algal blooms [145]. Beyond these outcomes, the "unknowns" of new diseases, the recurrence of "old" diseases, the worsening of drug resistance, and the steady increase in elderly patient numbers indicate that there will be enhanced requirements for sustainable medicinal agents in the next 25 years and beyond. Detailed estimates of these likely needs are based on a new, comprehensive set of health and environmental other metrics for 204 countries and territories [146]. The global pharmaceuticals market was expected to be about $1.65 trillion in 2024 and grow at an annual rate of 6.12% to reach $3.12 trillion by 2032 [147]. The sustainable origins of these expanded resource requirements for the next 15-20 years will necessitate a detailed evaluation to assure intact supply chains for patient benefit as transitions in sourcing and geographic needs occur.

Medicinal plants are of health beneficent and economic significance locally and nationally for many countries and the individual corporations and communities within them, and their use is projected to expand steadily in the future [148]. The annual global market for traditional medicines, dominated by China and India, is estimated to be $550 billion by 2030 [149,150]. These two countries are also the prominent users of medicinal plants in their well-established, traditional healthcare systems [151,152]. The European Union is the largest importer of medicinal plants at about 400,000 tons per year [153,154]. However, the biodiversity that underpins the medicinal plants in these systems and their availability is experiencing serious environmental, over-harvesting, and investment challenges regarding cultivation strategies to maintain access [155]. Subsistence support, financial and technical, for sustainable medicine practices in rural communities are urgently needed to develop an economic base for scientifically assessing, standardizing, and marketing traditional medicines [156].

Environmental change in its several forms is having a significant impact on the accessibility and metabolite profiles of medicinal plants, and survey studies were reported for medicinal plants in Thailand [157], China [158,159], Pakistan [160], West Africa [161], South Africa [162], and the Himalayas [163,164]. Since 2009 [165], there have been specific discussions presented [166-170], including a generalized, scientists' warning article [171], focused on the environmental threats to habitat and the resulting modulation of metabolite profiles of medicinal plants. A major issue which complicates any assessment of impact on health that for relatively few plants used in traditional medicine or phytotherapy are the bioactive metabolites known definitively. This makes the correlation of a changed metabolite profile to an altered biological response very challenging indeed.

A study in Indonesia summarized many of the environmental impacts on medicinal plants [172]. As a megadiverse country harboring three of the 25 global biodiversity hotspots and with an estimated 10% of the global flora used medicinally, maintaining access is a critical healthcare factor. Using different greenhouse gas emission models for 2050 it was calculated that over half of the current medicinal plant distribution area would be lost, and for some plants up to 80% of their growing areas would disappear. As a result, twenty medicinal plant species were identified as priorities for conservation efforts [172]. It is important to be very clear at this point, once again, about “time”. The Kew plant status summary [97] indicates that there are 28,187 medicinal plants recorded. How many of these plant species remain? Where are they located? What is their population distribution, and can that be determined through drone access? Which ones might be deemed “sustainable”? What is their potential to replace synthetic medicinal agents and natural resources as they become inaccessible, or are metabolically unsuitable?

These are mostly unknown, yet vital, factors to assess the demographics of the most important medicinal plants for bioprospecting within a country as one aspect of a local or regional replacement medicines initiative. Time is critical to establish answers to these and related questions to conserve the resources. The correlating awareness is that the time has long passed when research is justified on a plant because it is a “medicinal plant” that hasn’t been studied previously. That time passed in the 2000s, if not earlier. To be clear and realistic, most medicinal plants will never be studied chemically and biologically for their metabolite profile spectrometrically or their reported use with a relevant bioassay. Consequently, AI/ML-driven prioritization, based on the analysis of prior studies of related plants, metabolites, and bioactivity, has a fundamental role to play as research plans are developed.

Within the next 20 years, humanity will have to rely very heavily on these renewable resources for health care and biological agents, as the transitioning processes from oil, and eventually coal, occur and then affect the chemical supply chains for pharmaceutical synthesis and natural product development. Eventually, possibly around 2055, this non-negotiable, inevitable reliance on wholly sustainable resources will engage and persist for as long as humanity survives. Much needs to change quickly philosophically, scientifically, technologically, financially, and through structured sustainability initiatives to embrace the reality and respond to those requirements.

One of the foundational, plant-related data points of Medicines Security is to know from where a medicinal plant can be consistently sourced and standardized [25], especially if it has not been transitioned to a sustainable commercial crop [173]. What does this mean for a multicomponent medicinal plant remedy of say 14 or 20 or more medicinal plants if one or two plants are not available? What are the implications for the manufacturer and for the treatment expectations of the patient? Is it still a regulated and marketable product? What plants can be substituted for those not available? And then what are the experimental sciences required to meet local regulatory requirements? The answers, and consequently the strategy, for the future are quite clear. Open databases are needed which can help address these availability, phytochemical content, and biological response issues in terms of source locations and assess and establish the local intellectual property rights issues associated with new sources of needed medicinal plants for regulated products.

To accomplish this major transition in the primary function of natural product research, namely, to meet anticipated medicinal agent needs on a global basis, a high level of diverse plant knowledge and botanical, chemical, and biological expertise will be required in each country to decide what should be conserved, and what cannot. For many countries, plans for developing this expertise in the next few years through collaborative training programs will be required. The time has long past (think 1960s-1970s) when a broad based, global medicinal plant conservation effort was feasible. Selectivity, experimentally based, for which medicinal plants are the highest priority for conservation and the development of sustainability will be crucial. Plants know no boundaries for thriving in a healthy environment, thus a threatened or endangered plant in one country or region may be readily available elsewhere and become an economic asset. One can expect that regional trade in those sustainable, analytically acceptable, medicinal plants will become an important enterprise. That will require the development of harmonized regional regulations for medicinal plant registration and standards for pesticides, insecticides, heavy metals, and other contaminants and adulterant materials. The microbial sourcing of sustainable bioactive natural products through the expansion of a variety of synthetic biology approaches will be essential for developing new clinically significant compounds, as well as optimizing the availability of established metabolites for enhanced global availability, particularly in the context of overcoming multidrug resistance [174,175].

5.2 Natural products and human well-being

As humans, at least seven aspects to human well-being beyond physical health are recognized including emotional health, social connections, economic stability, purpose and meaning, creating and maintaining a quality environment, and opportunities for continuous learning [176]. Integrating these concepts of well-being with a balanced approach at the nexus of the natural world and the impact of technology is important for the individual, for relationships, and, by extension, for the broader health of the society. Our scientific activities for the future must embrace R.E.S.P.E.C.T. for nature as it remains fundamental for many aspects of well-being, and for the development of a supportive and regenerative environment which will form the basis for the long-term, sustainable sourcing of medicinal and other plant-derived agents for well-being. R.E.S.P.E.C.T. is an acronym for "**R**ealizing that **E**arthlings **S**ucceed by **P**reserving the **E**nvironment and **C**ultural **T**raditions". At the same time, it is apparent that our contemporary world is dangerously out-of-balance environmentally, economically, health-wise, emotionally, and technologically [8,26,177,178]. Major financial investments (well beyond those of COP29!) will be needed to attempt to evolve a balance between a technology-based society with the various elements of holistic Gaia that are under threat. Contemporary transactional destruction of the environment and non-renewable resources for a profit motive continuously raises the financial bill for the future. Financing of an alternative pathway requires a different "intent".

"Intent" in this situation requires awareness of the needs of future generations, and of the reality and reverence for the world "as is". A profound global intention to maintain, replenish, restore, and enhance what can be left for our descendants is a base-line parameter [26]. "Development" initiatives, including evolving natural product research programs, therefore require an assessment for their impact from a holistic perspective as a non-resource depleting, restorative, regenerative activity for humanity and for the natural environment [26]. Doing so brings authentic and meaningful respect for the lifestyles of future generations and the world *they* will continue to borrow from *their* descendants as Chief Seattle recognized 170 years ago. As each day passes without major behavioral change at all levels of local and global society towards one which acts beyond sustainability, the closer we move towards a catastrophic E.D.G.E. [2,3].

5.3 The E.D.G.E., Earth's tipping points, and beyond

The E.D.G.E. is an acronym for "**E**xperiencing the **D**isaster of a **G**utted **E**arth". That state would reflect a time when the critically needed renewable resources for continuing the societal *status quo* or for new bioprospecting initiatives, including for replacement medicinal agents, are no longer available due to over exploitation or environmental factors [2,3,18,121]. Such a calamitous manifestation may apply to non-renewable fossil fuels, such as oil and gas which are projected to "run out" (i.e., be very seriously depleted) by 2057, or to medicinal plants which have been acquired continuously from non-sustainable forest or mountain resources, leading to overharvesting [25].

The term E.D.G.E. also embraces how close humanity is to five, globally accepted and highly impactful, tipping points: i) the collapse of the enormous ice sheets in Greenland and the West Antarctic [notably the Thwaites Glacier (*vide infra*)] [52]; ii) the widespread thawing of terrestrial and marine permafrost (releasing stored methane gas); iii) the dramatic bleaching (currently 83.7% globally) of the coral reefs in warmer, more acidic waters [90,91]; iv) the weakening of the oceanic circulation in the North Atlantic, the Atlantic Meridional

Overturning Circulation (AMOC) [179]; and v) the timing of continued accessibility of fossil fuels [180]. Alarmingly, the recent five years have brought unprecedented awareness of the fragility of personal and societal well-being though diminished global health [181]. In addition, dramatic, unforeseen, and rapid environmental changes are being witnessed almost daily in some areas of the world. Contemporary civilization is witnessing a new global reality. Humanity, individually and collectively, may not like that reality, and may wish there was another pathway; the "old" one! However, it is now *the* "inconvenient truth" [182] and, as the UN Secretary General indicated in late 2024, we are almost out of "time" [46].

Status reports on Earth, also presented in late 2024 and 2025, discussed eight major areas of concern for the future [2,3]. Namely that, i) humanity is closing in on several planetary tipping points (*vide supra*); ii) the global climate is changing faster than climatologists expected for reasons that are unclear; iii) the Antarctic ice sheet shrank to its lowest level in 2023; iv) 2024 will be the warmest year ever recorded; v) the gaps in various aspects of economic inequality, locally and globally, are widening; vi) although slightly reduced, rainforest, and therefore biodiversity destruction for arable farming, remains a major issue; vii) globally, weather events are increasing in intensity; and viii) although the global population is still increasing, the rate of increase has slowed dramatically, from 2.22 in 1963 to 0.87 in 2024 [48].

There is another tipping point to be examined, one derived through anthropogenic inaction as time goes by. It is this. There remains an intense struggle in certain parts of the world with the reality of environmental change as a scientifically established fact for all humanity that must be addressed, very urgently. An authentic acknowledgement is needed, globally, that indeed this reality is not a "hoax" or a "scam". Societies, in their thinking and their actions, must not go backwards to the halcyon days of the 1970s, or act as though it were that era through the continuous sanctioning of new, non-renewable, fossil-fuel explorations. The situation is anthropogenic, and it is very real. It is occurring before our eyes now. It is the responsibility of humanity as one of the biological components of Gaia, impacting all the other components of Gaia, to act to save every component. It reflects the global interconnectedness of the "web". It is the positive tipping point of a deep global acceptance that "People of Earth, we have a problem!" Compared with the desperate need for deeper philosophical, scientific, practical, and financial commitments towards dramatic actions, humanity seems to be entering that healthy place of awareness, acceptance, and acknowledgment. Currently, even those who do recognize the depth and seriousness of the issues [2,3], are in a place of "strategic uncertainty", i.e., chaos. Not knowing what to do to be impactful locally and globally. And there is the ever-present confluence of "time".

Imagine this predictable scenario, that with a higher level of acceptance the next step would be to answer the questions "How bad is it? Will it get worse?" Then comes the realization and acknowledgement that this is a really, really bad situation, and that there is no plan(et) B; there never was! Several years later, the question will evolve as "How much will it take to fix the problem?" Followed by: "But, we don't have that money for restoration." By this time, it is 2055. "What you say!! Now it's too late!!!" Will that be the journey of humanity and this remarkable organism that is Gaia? Will that be your destination, in your lifetime? Remember, the UN Secretary General has already announced to the world "We are out of Time". Is there an ambiguity in that statement that precludes comprehension? Will humanity have tipped over eventually to an acceptance requiring action too late, not realizing that there is, at that point, insufficient time, money, and resources to ameliorate (cannot reverse!) the ecological direction of the "star ship", as the Earth maintains its' circles around our consummate energy source?

To be abundantly clear, once each tipping point is passed, there is no going back, as concluded for the bleaching of the coral reefs [91,183]. Passing most of the tipping points would be utterly catastrophic for Earth and the survival of humanity [2,3]. There is no reverse gear for any of the tipping points to take the planetary environment back to the 1980s or even the early 2000s. Those halcyon days of overuse, excessive waste, and unmitigated resource depletion have brought us to a new place in a very different world. From the perspective of global medicines those two dominant myths regarding the assumed continuing availability of the plants, the marine resources, and the chemicals for extraction and synthesis must be relinquished. Now is the time to develop bioprospecting initiatives to provide and assure that healthcare is firmly based on wholly sustainable medicines for the future generations.

What of the “time” beyond each of the tipping points as they are successively breached? There are clear indications that at least seven major impacts will then transcend Earth [2,3], namely: i) Climate feedback; ii) Continuing losses of biodiversity; iii) Food insecurity, iv) Fragility of water supplies; v) Proliferation of diverse human and animal diseases, vi) Collapse of economic systems and resulting mass migrations of affected populations; and vii) Ocean acidification. To which we should now add “medicines insecurity”. The future demands contemporary strategies, planning and funding for long-term resource replacement and replenishment initiatives at established centers of excellence. Who will take responsibility for their initiation scientifically, financially? Locally? Globally?

As noted, a quite different pattern of thought and creativity is needed to overcome the very serious issues medicines supply chains will face in the coming 20-30 years, especially if further tipping points are closely approached or worse, breached. Already, for several reasons, including profitability and supply chain limitations, about 270 approved medicinal agents in the United States are not available for patients according to the United States Food and Drug Administration (USFDA) website [184]. In the summer of 2024, there was a critical shortage of cis-platin in over 90 major US cancer centers. The inaccessibility of this widely prescribed cancer chemotherapeutic agent caused serious complications for continuing cancer patient regimens [185]. The persistent recalling of approved drugs by manufacturers is summarized at the US FDA website [186].

As a very high priority, a healthy population requires a high focus on the patient and a concerted response to their continuous and expanding needs for accessible medicinal agents [98]. It is another core perspective of Medicines Security in which, ethically, the quality and performance of the product require preference over corporate profit. From a health beneficent perspective, what are the science-based qualities that all patients desire from medicines now and for the future? Elsewhere attention has been paid to this discussion [25] for prescription and OTC products, traditional medicines and phytotherapeuticals, and the internet provision of plant-based medicinal agents. Quality, Safety, Efficacy, Consistency, and Accessibility (availability and affordability) (Q.S.E.C.A.) have been identified as the critical attributes of each preparation a patient relies on for a healthcare purpose, irrespective of the origin, natural or synthetic [98,187-189].

Unfortunately, for most of the traditional medicinal agents in use around the world the local regulatory systems are not close to establishing acceptable standards for those attributes to be realized for a product in the marketplace for the benefit (security) of the patient on a lot-to-lot basis [190-192]. For the years ahead, in 2040, 2050, and beyond, how will these quality concerns of performance be addressed? The days of talking and excuses are over. Actions are needed through Triple Helix-based (Government, Academia, and Industry) collaborative initiatives, raised to the level of the Quintuple Helix through the additions of societal impact and long-term sustainability [99]. The applicable sciences and technologies must be implemented to focus on and assure a “healthy future” based on Q.S.E.C.A. for *all* products intended for medicinal and biological purposes. That is one of our responsibilities [188,193]. In 2025, it is unconscionable that this fundamental healthcare need for a consistent product that “works” clinically must still be addressed from ethical and scientific perspectives.

In part, a major barrier which limits progress on these issues for most of the world relates to pharmaceutical companies and regulators in the North dictating what qualifies as a “drug” and the projected safety and efficacy standards a medicinal agent must reach before final approval as a prescription product. These are outdated and unrealistic global standards for enhancing the impact of traditional medicines in an integrated health care system for most of the world, at several levels, including the extent of very expensive clinical trials. Progress in the development of standardized safe and effective preparations and delivery systems based on traditional medicines is *not* due to a lack of bioactivity, as some believe, or to the available facilities or the expertise to carry out meaningful determinations. It is the absence of intent and thus requisite funding. The natural product sciences must generate a clear intention to attract investment to apply the processes for quality improvement that will serve community healthcare needs, including affordability and availability. For the future of wholly sustainable healthcare around the world, there is no option. Interestingly, the USFDA, which has the most stringent processes for prescription product approval, has very lax regulations regarding what the patient ingests as a traditional medicine or dietary supplement, relying on a self-policing industry for the quality control of products, while focusing on the label. [194]. Also ironically, and in another context and with profit not healthcare at stake, but with the clear intention of enhancing "quality", the world has been here before.

The management specialist W. Edwards Deming brought that intent, spirit, and application of enhancing "quality" to Japanese manufacturing in the early 1950s, which, over many years, changed how the world viewed the quality and design of Japanese products [195]. As indicated, the natural product scientific world will never have either the time or the scientific and financial resources to create prescription products from thousands of traditional medicines. That is a fantasy. What can be achieved [196] is to raise the quality standards globally for what is (and will be) in the marketplace for the patient through the selective establishment of Q.S.E.C.A. to the clinically most important and sustainable products. In the process, a third class of safe and effective natural product medicinal agents will be created [197]. Medicines must also be developed for the local and global diseases (e.g., MDR, dengue, Chagas' disease, etc.) for which no drug is presently available or where existing drugs have undue side effects. Aggressive actions are needed so that overall, most of the world will be acquiring sustainable quality medicinal agents as the population milestones of 9 billion and 10 billion potential patients are reached, and non-renewable fossil-fuels access has been significantly curtailed or has ceased.

To be very clear, for a country to rely on producing or importing synthetic drugs, including those on the WHO Model List of Essential Medicines [198] as a strategy for their Medicines Security beyond 2040 is not a rational approach. The caveat is that few countries in the world have the pharmaceutical manufacturing capacity, even from imported raw materials, to meet their local needs. Fewer nations can produce the required chemical precursors, and consequently their availability will continuously be under threat to exhaustion. Even fewer countries have the major pharmaceutical company capacity for the discovery, pharmacology, pharmacokinetics, formulation, clinical trials, production, and distribution infrastructure to support the complete pharmaceutical process based on sustainable natural product feedstocks. Whose responsibility is it to address these basic global medicine supply concerns? Forty areas for the future promotion and global development of traditional medicines were suggested to respond to this major health care issue under the framework of Medicines Security [25]. The UN Secretary General and the Director General of the World Health Organization might wish to consider initiating the next steps to protect this aspect of future health care for humanity from a wholly sustainable Medicines Security perspective.

6. STRATEGIES FOR THE FUTURE

The process for (re-)establishing a system for Medicines Security which is based on totally sustainable natural resources will require major re-thinking of the strategies and processes and the integration with a variety of technologies. That topic will be the subject of a further detailed discussion and only a brief commentary will be presented here. The arbitrary examination of plants, even those with a long history of use as traditional medicines, as a potential source for the development of new therapeutic agents no longer has a rational basis; these are fanciful dreams of bioprospecting [25]. That type of research is not in congruence with future healthcare needs for new and replacement biological agents. It is well-established that medicinal agent discovery programs from natural sources are mostly not synchronous with global disease needs, and some of the factors involved have been presented [199]. Re-engaging with a rational and sustainable approach *and* putting the patient needs first [25,98] requires deep reflection and realignment of intent for projected population modulations. Precious resources (natural, personnel, facilities, and state-level financial) must focus on selective, highly collaborative initiatives that represent nationally prioritized needs for either local diseases or to replace existing, but disappearing, medicinal agents, natural and synthetic. Following sustainability assessment, chemical and biological dereplication and metabolite profiling, data sets must be engaged in all prospecting efforts to avoid the unnecessary (and wasteful!) scenario of isolating a known, moderately active metabolite, unless the specific new bioactivity of the known metabolite is unreported and is of high interest [200,201]. Unfettered claims of potential clinical effectiveness from a single *in vitro* assay are hyperbole, confound credibility, and negatively impact respect for the veracity of the natural product sciences.

In the past, natural resources, particularly terrestrial plants, were viewed as a largely unexplored source of bioactive compounds, theoretically serving as a potential source of new biological and therapeutic agents using contemporary techniques such as *in silico* modeling [202]. A radical change in fundamental thinking is required to serve contemporary needs, future disease threats based on climate change, newly emerging diseases, and supply chain concerns. Seeing nature as *a* "potential" source of medicines for a time beyond 2050 does not embrace the reality of reaching fossil-fuel boundaries. Nature in its breadth and depth must now be viewed as *the* critical sustainable resource for bioactive metabolites, reagents, and solvents in response, where prior cultural and experimental information is evaluated and prioritized toward local needs [203]. Within the next 10-20 years, a major transition must occur towards a substantially greater reliance on sustainable resources for the provision of biological and medicinal agents [25,98]. Eventually, probably around 2070, an intact "return to nature" base for medicinal agents will evolve as the *only* pathway for humanity as the last supplies of non-renewable, fossil-based chemicals (i.e., coal) for the synthesis and processing of medicinal and biological agents are being dissipated or will have become unaffordable for all except the wealthiest segments of the developed world.

In this scenario it will be necessary to have explored, previously and avidly, the prioritized global development of natural sources for sustainable new agents to replace those natural and synthetic materials no longer available, and to have sought sustainable and stable enzymes to conduct high yield, chiral (if applicable), chemical reactions on a wide range of substrates. This exploration will be driven by the need to eliminate rare metal-based, single use, expensive reagents and catalysts. If the enzyme reagent does not require isolation from its renewable source, the economics and the simplicity and reproducibility through reuse of a" greener" process are further enhanced. One such example is the direct use of vegetables as chemical reagents, most notably for the reduction of a prochiral ketone to afford a chiral alcohol at room temperature after 72 hrs. in exceptional yield and with very high enantiomeric excess [204]. Among the effective "reagents" are carrots, cassava (manihot), coconut juice, and sugar cane, which can remain active for up to six catalytic processes. Esters and lactones are not reduced. The reaction replaces the use of single use, chiral hydride reducing agents, rhodium or ruthenium catalysts, and chiral metal or hydroboration reagents. It can serve as a model for the identification of desirable "simple" chemical transformations utilizing sustainable, plant-based reagents.

As the studies of the biosynthesis of plant and microbial metabolites clarify exquisite reaction pathways, specific enzyme processes are becoming evident through biochemical demonstration. The ability to determine the substrate specificity and to selectively modify amino acid binding sites allows the development of enzymes with a broader substrate space and binding capacity, as the genes encoding for the enzymes conducting these (bio)synthetic steps are unveiled. In addition, more investigations are necessary, without isolating the enzymes, to explore the use of crude plant and microbial preparations for a diversity of common organic reactions, including functional group oxidations and reductions, C-C, C-O, C-S, and C-N bond forming and cleaving processes. Thus, nature should also be viewed as a source of stable and sustainable "chemical reagents", as enzymatic, multiple step pathway sequences are constructed towards AI-generated targeted products which have been identified and optimized through ML algorithms. These efforts will be crucial for developing the sustainable supply of replacement medicinal and biological agents, providing scale-up processing can be achieved on a consistent basis.

6.1 Medicines security

Facets of the term "Medicines Security" were presented at various points earlier in this review. The concept was initially described in 2017 [98] and subsequently refined [25]. As outlined, unlike foods, mystifyingly, there is no corresponding international agency for assuring the global availability of quality synthetic and natural medicines. Maintenance of supply, resilience, and the quality and the consistent integrity of prescription, over the counter, and the capacity to utilize standardized local or global traditional medicines, are of significant international concern, especially for the materials the patient sources online. WHO has commented on the widespread fraud of traditional medicines and phytotherapeuticals [143], and other research studies of market products continue to add context and depth to this huge global problem for patients in selecting a medicinal agent to be trusted [190-192,205,206].

The presence of undisclosed excipients and diluents in botanical extracts has also been identified as an important quality control issue, further undermining the anticipated clinical response for the patient [207]. Two primary deceits were noted in this study. The first was that of extreme levels of dilution of a plant extract with non-declared materials; maltodextrin was found as a common diluent. Secondly, the re-sale of the marc of an extracted plant without indicating an applied previous extraction was observed. If the former extractive already contains the bioactive metabolites for the indicated purpose, then the marc will not show the biomarkers on analysis and will be of no biological value for the clinical intent of the patient. Examples of these practices included ginkgo [208-210], black cohosh, echinacea, and milk thistle [211], St. John's wort [212], and Andrographis and Boswellia [213]. Even techniques for the deliberate deception by a manufacturer to preclude accurate phytochemical analysis have been exposed [214]. This virulent level of fraud utterly decries the concept of putting the needs of the patient for a high-quality, safe, effective, consistent and, from the patient perspective, secure product first [25]. Health-related products with a broad spectrum of claims are frequently beyond regulatory control prior to purchase and are typically only assessed randomly or if a health crisis occurs [215]. The limited access to the cancer chemotherapeutic drug cis-platin in 2024 (*vide supra*), revealed a different false assumption, namely that the manufacturers of a medicinal agent will continue to operate facilities which meet GMP standards [216]. When product manufacture is halted due to the inadequate enforcement of practices and protocols, including the recall of manufactured agents due to contamination [186], the supply chain is automatically disrupted and the security of availability for the practitioner and consequently the patient is lost.

What does the term "Medicines Security" mean in context, and how is it central to putting the patient first in developing plans for both synthetic and natural medicinal agents? The concept is part of a much larger concern, the development of carbon-neutral (net-zero) chemical, pharmaceutical, and bioactive plant processing (dietary supplements), and replacing selected materials in the myriads of fossil fuel-derived chemicals in the cosmetic and fragrance industries [215]. Germany is actively engaged in planning for their chemical and pharmaceutical industries to be independent of non-renewable resources, with a variety of models proposed for 2045, and notably, manufacturing plant conversion cost estimates are already being developed [217].

Medicines Security [25,98] acknowledges the priorities of the patient for dietary supplements, traditional medicines, and cosmetic products to have all the scientific aspects of quality, safety, efficacy, consistency, and accessibility (Q.S.E.C.A.) applied [187]. Wider perspectives for medicinal agents, irrespective of their source, begin with an indication that the preparation will be sustainably sourced and manufactured under GMP (eventually in a carbon-neutral manner) to be consistent. From a medicinal plant perspective, the supply chain begins with the harvesting location for the plant material and the resilience of the integrity of those locations over time. That forms the basis for the initial, reproducible quality control and analytical steps in developing a consistent product for the patient. The impact of environmental change through drought, flooding, fires, pollution, and salination of the soil will modulate the required metabolite profile in a manner that is not predictable and may well differ season to season, as well as annually. Securing consistency in a starting material for processing will probably be a significant challenge in communities vulnerable to environmental transitions and will have an important impact on how to exercise rational regulatory control as diverse metabolite profiles are identified for products from different acquisition sites at different times of the year.

Security for the patient also focuses on product authenticity and correct dosing (i.e., not diluted), and presenting to the patient a product that is not adulterated with synthetic agents or contaminated with other plants, or pesticides, or heavy metals (Hg, Pb, Cd, As). Quality, safety, and effectiveness must be maintained securely through step-specific monitoring from the point of origin for consistency overseen by an immutable, resilient, quality-focused informatics process. Another fundamental concept of Medicines Security reflects what the patient in the marketplace experiences and rely on. Namely, that the authentic product will be accessible, i.e., that it will always be available and affordable in the context of the prevailing local economy. The immutable nature of the data associated with the quality of a particular product on a lot-to-lot basis, delivered through a QR code, should provide a focused timeline from the point of origin to the point of purchase. That accessible information should help allay patient concerns regarding product authenticity, which is a major global issue, and enhance trust [143].

As the production of many synthetic medicines diminishes with the ongoing transition process from non-renewable to sustainable sources, patients in the future will also need the security of knowing that the bioprospecting for new medicines, e.g., for drug resistant organisms, neglected diseases, for the changing levels of disease prevalence from climate change, and for medicines replacement are each recognized and are being pursued. Additional security requirements relate to the applied sciences and technologies substantiating the product and its marketing, including that all the experiments conducted on a lot-to-lot basis were appropriately controlled and the data interpreted correctly. Finally, the patient wants the security that the labeling (including recommended dosing) and marketing of the product with respect to any claims for treatment by a registered product are ethically based and are authentic with respect to the biological assessment of the same standardized material being sold. The functional claims used for marketing must not reach beyond the available experimental and clinical data.

With respect to the plant-derived medicines in clinical practice, there is the vast topic of extended sourcing. Where are the plants, and how abundant are they in the growing area? The provision of a commercial plant preparation assumes continuous access to all the plant(s) in the composition. That represents a significant challenge for a complex plant matrix. Is that feasible if the plant material is wild-crafted, or will most major medicinal plants now require cultivation protocols to be established? Is that even possible for all the plants involved in a 12 or 20 or 36 medicinal plant mixture for an extended period of 5-10 years? If not, what are the research strategies to be implemented to assure product continuity, including at the regulatory level, for patient benefit? Global Information System (GIS)-based models have been presented [218,219] which can analyze suitable sites for the potential cultivation of Chinese medicinal plants. If the plants are wild-crafted are the locations for harvesting well-established for the long-term and not under direct environmental or anthropogenic threat? If the locations are not secure, can locations identify from herbarium specimens be used to provide alternative potential sites for acquisition and yield a metabolically comparable preparation? And when the cultivations' location changes, what happens to the metabolite profile, and the associated biological outcomes?

Another important consideration for the future of sustainable natural products relates to the cosmetic and fragrance industries, and the sourcing and integrity of their feedstock materials in the next 20 years and beyond [220-223]. Even though fragrances account for only 0.077% of the hydrocarbons market at 640K tons/year [224], a challenge was laid down in 2021 for Unilever Home Care, Health, and Wellbeing to shift to 100% renewable and 100% biodegradable materials by 2030 [225]. This will be the subject of a future discussion.

6.2 Effects of defossilization on chemical resources

"Transitioning" towards defossilization for energy requirements was the most important outcome of the COP28 meeting in Dubai in December 2023. However, the absence of timelines or benchmarks or financial proposals undermined the planning initiatives required to identify alternative sources for the dissipating fossil fuel-based assets. This includes the continuous supply of organic chemicals and reagents for the synthesis of approved biological and medicinal agents. By the mid-2050s, when oil has been almost exhausted, and coal sourcing will likely be heavily limited with respect to the 2045 net-zero environmental controls [217], what will be the renewable feedstocks, and the respective costs of the solvents and chemicals required for the manufacture of synthetic medicines at that time? With medicinal products experiencing a steadily declining access to vital processing and precursor supplies in the next 20 years, what is the projected economic impact for the manufacturer and by extension, the patient? Where are the deep-seated reflections on the sustainability of sourcing and quality control supply chains? Developed strategies, as a global requirement for healthy people on a healthy planet, will require assured sustainable medicines access and resilience, focused especially on the agents on the WHO list of essential medicines chosen for their country.

Alternative synthetic sequences for the selected medicinal agents will require creativity and time for new, wholly sustainable, pathways to be developed, reapproved, contaminants determined, and the re-establishment of the comparability and bio effectiveness of the "new" product. If reformulation of the product is also necessary, a limited clinical trial for pharmacokinetics, bioavailability, and effectiveness will probably be required. The time for evidentiary determination, assessment, and approval will be the controlling factor for entering the replacement into clinical practice. Within the next 15-25 years, for how many of the currently approved pharmaceutical agents will this process be economically and scientifically feasible? Many of the currently approved products will become inaccessible synthetically based on the absence of sustainably sourced precursors and reagents, or the processes themselves will become economically not feasible, or the development and approval process will be too long (too late!) Strategies for accessible, temporary and long-term, sustainable replacement agents will become the highest priority for medicinal and biological agents. For the next thirty years and beyond, these will be very challenging and exciting collaborative research opportunities for synthetic natural product and medicinal chemists and biologists to develop pharmaceuticals and other medicinal and biological agents (e.g., pesticides, insecticides, etc.) with a net zero profile and a consistent, completely sustainable supply chain.

6.3 Evolving challenges and L.O.V.E.

Since the evolution of humanity in the Paleolithic Era 3.3 million years ago, reliance on the assets of nature and potentiating new discoveries with a high level of functional utility has been a consistent pathway for sociological, intellectual, and more recently scientific and economic development. Until the very late 19th century when Bayer first introduced the semisynthetic drugs heroin (diacetylmorphine) in 1898 and aspirin in 1899 [226], *ALL* medical and cosmetic agents originated in nature in their entirety. The first totally synthetic drug to be marketed was prontosil in the 1930s for bacterial infections [227]. This earlier historic, total reliance on nature for medicines, paused through the magnificent synthetic efforts of medicinal chemists to address many important global disease issues in the past 125 years, represents the greatest chemical achievements for the survival of humankind. That total reliance will have to return to meet patient and consumer needs and maintain contemporary lifestyles beyond 2055 [228-230]. Before the sustainability concerns arose for continuing fossil fuel-derived chemical resources, there was barely a thought about dwindling assets for medicinal chemistry, and the need for alternative strategies. Now all that has changed, and thus, the fundamental strategies for assuring supply chains must also change. Transitioning away from the ethos of synthetic medicinal chemistry as *the* solution for new medicinal agents will result in a focus to the dedicated sustainability of natural product sourcing over the next decades [25]. This deep-seated, paradigm shifting, philosophical change and the associated experimental scope across the sciences will present an enormous new series of challenges for the provision of medicinal agents for the duration of humanity. That demand will never stop. And it is that reality which requires acceptance and action. Reticence will not result in Medicines Security for the patients of Gaia.

In this scenario, the optimization of all available natural resources to avoid the depletion of assets over extended time is crucial. There is a need to reach the net-zero provision of natural medicinal agents from two perspectives. For the drug manufacturers, the formation of products with net-zero greenhouse gas emissions within 20 years must be matched with detailed analyses of the feedstock materials and their replenishment. For synthetic chemicals, that shift will be based on continued access to coal-derived chemicals for a period, subsequently replaced by the new chemical sourcing of all foundational chemicals from a circular economy optimizing “waste” (*vide infra*). For natural product-derived medicinal and biological agents, the key will be the sustainability of the sources in a natural or highly controlled environment and their replenishment on a continuous basis for future generations. A major expansion of current practices, and the challenge to acquire and develop the space to grow those resource materials will evolve as another significant economic factor. Which brings us to L.O.V.E. - a fundamental facet of life going forward, as it has been throughout humanity.

It is established that other parts of Gaia, over the millennia, have been the terrestrial and marine resources for the valuables of Earth available and cherished today by humanity. However, the non-renewable resources of Earth have boundaries of supply which are impossible to replenish, ever. Coal dates from the plants of 260-390 million years ago, oil mostly from the marine plankton of 70-200 million years ago [231]. Crossing their supply boundaries are now realistic events. Alternative sourcing for medicinal and bioactive agents could originate from either new sustainable natural sourcing, new uses beyond the original natural resource, or the transformation of biowaste (*vide infra*) to produce “starter” chemicals for very “green” organic synthesis. The core implication is that optimization is essential throughout the resource supply chain to potentiate the accessibility of the final product for the patient/consumer. New thinking and new processes will be imperative, and some examples will be presented shortly. To bring focus and embrace the importance to these concepts the acronym L.O.V.E. was developed [25].

The pathway of L.O.V.E. (**L**earning to **O**ptimize the **V**aluables of **E**arth), is, in reality, a long-standing, basic tenet of humanity’s complete historical relationship with nature. It is how humanity has converted weeds and forests into crops, foods, furniture, shelter, natural medicines, and all the other gifts derived from nature we experience every moment of every day, including energy. Now, optimizing what remains or what resources can be replenished or enhanced has evolved as the dominant requirement for managing the resources of Gaia for the future generations [25]. It is important to understand, as the primary, enduring requisite, that these activities of optimizing renewable resources, embracing L.O.V.E., is no longer an option.

Optimizing, without overstepping, the boundaries of Earth’s resources is the only journey for preserving, replenishing, and restoring (as avidly as possible) the medicinal resource requirements for the ~9.5 billion Earthlings of 2050 and beyond. Initially, those resources will be blended, in a very limited way, with renewable and recyclable resources. However, continuity of access will require a vast array of new, creative bioprospecting and synthetic endeavors as the rational access (think recovery costs!) to non-renewable resources diminishes. The precise timeframe for implementing those processes is unknowable at this point; only that they will be required at the latest around the mid-2050s. Creativity to develop the circular (bio)economy which is central to the optimization of a particular resource. A plant, such as a palm tree, must be seen holistically as having vast potential for broader uses than the palm oil. The same is true for many mega crops where massive amounts of "waste" are continuously generated which have substantial chemical potential to be optimized as sources of small molecules for modification [232,233].

Many examples of L.O.V.E. in the natural product sciences already exist when viewed in terms of potentiation of biological activity or finding the best pathway for a synthetic process. For a microorganism, modifying the genes in a biosynthetic pathway to alter the diversity of substrates and therefore products, enhancing the yield by eliminating regulatory genes [234], or eliminating functional groups to avoid toxicity [235] are among the evolving approaches for optimizing the yield of a needed metabolite [236]. For a medicinal plant, once the bioactive metabolite(s) for a particular activity are identified, enhancing the yields of bioactive metabolites in an individual biomass becomes a goal. Using vegetables, and not heavy metals, as recyclable chemical catalysts (*vide supra*), utilizing biowaste for enzyme and chemical production, finding new uses for established, sustainable metabolites, and transitioning wild-crafted plants to high-yielding agricultural crops, among many other initiatives, recognizes that historic single uses for established, sustainable natural resources must now be explored intensely through targeted, well-financed development strategies.

6.4 Whither "Waste"?

"Waste" has several implications in English. There is "waste" in terms of goods and food. There is "waste" in terms of money, of effort, of excessive indulgence, the "wasting away" of an ageing body, and there are the seven "wastes" of lean manufacturing [237]. There is a profound sense of "waste" in many contemporary natural products research programs. Are they focused on personal interest or societal need, for example? These efforts require a much deeper consideration and reassessment of how they will respond to patient and societal needs deploying sustainable natural products going forward. Most significantly for natural products and their role in society, there is the concept of "waste" in terms of time. Are natural product research programs meeting societal needs currently, or have we been "marking time", with minimal direct benefit to health care and well-being for the past 30 years, given the level of investment? There is significant global pressure to assure access to high-quality existing healthcare products and, because of the narrow discovery focus of Big Pharma, to develop sustainable new products to fill established niches of health care and biological need, including MDR, neglected diseases, insecticides, herbicides, etc. How that paradigm is changed, individually and collectively, for the patient and for Medicines Security offers significant creative opportunities [98], and will require major long-term strategic investment, locally and internationally.

Returning to the concept of time-wasting and its relevance in the present global situation, there is a powerful literary example. Richard II, in Shakespeare's play from 1595 of the same name (Act 5, Scene 5), aware of the power he had lost and the failure of his actions, laments, "I wasted time, and now doth time waste me. For now, hath time made me his numbering clock". The pertinent quote of the UN Secretary General on "time", notably "We are out of Time" was mentioned earlier. After 29 Meetings of the COP for Climate Change and 16 COP Meetings for Biodiversity Conservation it is immoral and irrational that this is really the situation for humanity from a time perspective. Having "wasted" time for so many years with endless talk and little investment let alone action, humanity is now facing the diminishing number of years of access remaining for essential resources. It is within this remaining time period of 15-25 years that the research for the optimization of renewable resources for sustainable bioactive products, including medicines, must be conducted. "Time", and its' passage, is now very much in control of our future. Human health and lifestyles have become its “numbering clock” as the years have passed, and they also may waste us away unless decisive actions occur very, very soon to avoid a healthcare catastrophe.

Regarding commercial goods and food, there is a well-honed expression, "Waste not, want not”. Perhaps it was (is?) an expression in your house, it was certainly in mine! Interestingly, it too originates from the late 16th century: “For want is nexte to waste, and shame doeth synne ensue” is from *The Paradyse of Daynty Deuices* by Richard Edwardes published in 1576. As the finite resources of the planet are diminished, and the boundaries get closer, L.O.V.E. requires a deeper exploration of the chemical potential for “waste”, lest future generations of humanity simply “want” what contemporary generations have. History will not reflect well on this delayed action response.

The population of Earth exploded from 2 billion in 1930 to 8.255 billion in late-2025, a period in which the W.A.R. on nature intensified. This W.A.R. is beyond the “war on nature” eloquently described by Rachel Carson in *Silent Spring* as: “But man is a part of nature, and his war against nature is inevitably a war against himself.” She was referring to the massive daily losses of biodiversity as the forests are transformed into urban dwellings and arable and range lands [7]. In the present context, this W.A.R. is an acronym for **W**asting **A**vailable **R**esources. As background, the average person in the USA produces about 1,800 lbs. of solid waste each year, ca. 33% of the world’s solid waste [238], and more than $218 billion is wasted on food in the USA each year [239]. For comparison, a person in China generates up to 396 lbs. of waste per year, and in India about 313 lbs. per year, depending on location.

The notion of “waste”, especially “biowaste” to be disposed of in a landfill, is passé. It violates a fundamental aspect of L.O.V.E., namely, the “optimization” of available natural resources, especially after they have been partially utilized [98]. “Waste” is the end point of the deeply ingrained, linear economy model: “take - make – use - waste”. Taking from Earth’s resources, making a product, using it, and then throwing what’s left away and replacing it with a new creation. Perhaps we can visualize **W**.**A**.**S**.**T**.**E**. as **W**atching **A**ssets **S**lide **T**ragically into the **E**arth without the optimization step that is critically needed when present and future generations must thrive within diminished, finite boundaries.

The annual ritual of new car models exemplifies this economic approach and continues to compel a sustainability quotient [240]. The practices of the linear economy are no longer acceptable as a pathway for sustainability and human survival [26]. Thinking and acting “beyond waste” to extended use optimization is essential. In stark contrast, a (bio)circular economy is not based on disposal after use, but rather on reuse, replenishment, and recycling [241]. Pointedly, these attributes reflect a very fundamental difference between profitability in the model of the 4IR and the sustainability and resilience presented by the 5IR. The appropriate response for the future can be highlighted in another way. Simply ask the question “What does nature do?”, dispose and ignore forever, or a find a new use? Regeneration in a new form is the clear response from the molecules of nature over billions of years. Every primary forest in the world, and many of the secondary forests are based on the gene-driven, regenerative processes of nature, and, over time, as Darwin first enunciated, the continuous diversification and speciation of the ecosystem [242].

The transformative thinking from a linear to a circular system of resource utilization recalls the German chemist August Kekulé who, in 1865, proposed that benzene, whose molecular formula was defying interpretation as a linear molecule, had a circular structure, mimicking the motif of the “ouruboros” of ancient Egypt and Greece. This mythological symbol represents the snake eating its tail, reflecting the continuing natural cycle of destruction and recreation. As observed several years ago, “We can extend that concept to the recycling of waste to reduce the rate of depletion of our planetary resources for future generations.” [189]

In a circular economy, which aims for a closed-loop paradigm minimizing pollution and carbon emissions [243], reallocation, reuse, repair, refurbishment, recycling, regeneration, and remanufacturing create systems approaches which have minimal inputs and leakage over extended time. These efforts will embody the essence of creative opportunity. There are vast chemical resources, natural and synthetic, which end their perceived useful "life" as either terrestrial or aqueous pollutants or as landfill waste, which are clearly not sustainable practices. In 2020, the European Commission established a *Circular Economy Action Plan* designed to establish a wholly sustainable product as an anticipated manufacturing outcome within the EU by 2050 [244]. One should anticipate that the products sold in certain economic sectors will, of necessity, be almost totally sustainable and fully recyclable, since a disposable outcome product would be regarded as a "failure" of that operational paradigm. In this scenario, the opportunities for natural product and medicinal agent research are substantial and challenging and will require significant creativity and investment. Biowaste materials are critical assets to be explored [245,246] as the originating sources for industrial enzymes, foundational chemicals, reagents [247], and materials for nano-fabrication, etc. through degradative processes [248-250]. Many countries will establish their own (bio)circular economy based on their local biowaste assets, e.g., the biowaste from the processing of nuts [251], the processing of the three main biowastes from beer production, spent grain, hot trub (high molecular weight proteins), and residual brewer's yeast, for other uses in the food industry [252], and the many uses for pineapple waste [253].

Globally, there is lignin waste, the most prolific aromatic biowaste material on the planet [249]. It includes the core 3',4'-dioxygenated-C_6C_2-phenylethyl scaffold within the polymeric material. This scaffold is present in several broad classes of biologically active natural products, including many alkaloids, coumarins, flavonoids, lignans, etc. Depolymerization of lignin has therefore attracted attention as a source of precursor chemicals for the synthesis of new products [254,255] and fine chemicals [256-258]. Some of the important processes and products from the depolymerization of lignin-cellulose materials to deliver foundational chemicals have been reviewed [259]. The acetal derivative of 4-hydroxy-3-methoxyphenylacetaldehyde, derived in very high yield from lignin through acid hydrolysis and ethylene glycol protection [260,261], can serve as a precursor for quinazolinones, tetrahydroisoquinolines, and *N*-phenethylindole derivatives [248,249]. Another interesting example is the pathway from lignin to the mild analgesic agent paracetamol (for a review of various biomass-based synthetic routes, see ref. [258]), which classically is produced at around 16,250 metric tons/year and valued at USD 130 million. The target intermediate was 4-aminophenol derived from the degradation of biomass from poplar and palm trees as 4-hydroxybenzoic acid followed by conversion to the amide, Hofmann rearrangement, and acetylation [258]. The potential to produce a broad range of significant chemicals on a commercial scale, including nanocellulose, oligo- and monosaccharides, as well as small molecules of interest has been reviewed [262].

6.5 Continuous growth and other pathways

The continuous growth of Earth's population, which is now being aggressively encouraged in several countries in the world (*vide supra*), leads to enhanced ethical challenges for any model that recognizes sustainability for future generations as a minimal paradigm for the journey of humanity. Indeed, these proposals serve to defeat or delay many of the SDGs, especially when economic success is tied to the widespread drive to enhance GDP annually [263]. However, ecological economics growth based on GDP is viewed now as an archaic measure of the well-being of a country, in part because it is a translational artifice, and not a reflection of the holistic, sustainable human development in a country, or indeed of Gaia [26,264-266]. The GDP of a country assumes that: i) a global market economy can continuously grow despite Earth's resource boundaries; ii) the current massive global social and economic inequalities are fully justifiable, and iii) considerations of climate and environmental change cannot (be allowed to) interfere with economic growth. These concepts of GDP are more aligned with the productivity-oriented Fourth Industrial Revolution rather than the contemporary emphasis on sustainability, human well-being, and resilience promoted by the Fifth Industrial Revolution [11,12,20,21].

Enlightened global leaders are aware of this paradox for an Earth with dramatic environmental change underway and non-renewable resource boundaries. Ursula von der Leyen, the President of the European Commission, in remarks at the “Beyond Growth Conference” in Brussels, Belgium in May, 2023, indicated that countries should halt their “addiction” to continuous growth as a goal towards an enhanced GDP. She went on to propose that countries move urgently towards sustainable well-being based on the known planetary boundaries. Adding “Only a sustainable economy has the resources to invest in a healthier and in a fairer tomorrow.” In many ways, the push for an ever-increasing GDP may be viewed as the **G**randest **D**eception of the **P**lanet, for the environmental and resource realities it attempts to mask from the impact of sustainability for future generations. Indeed, the notion of continuous economic **G**.**R**.**O**.**W**.**T**.**H**. may be considered as **G**rinding **R**elentlessly **O**nward **W**ithout **T**hinking with **H**eart.

The Thai social activist Sulak Sivaraksa in *The Wisdom of Sustainability* has described many of the consequences for humanity resulting from continuously expanding consumption and economic growth when coupled with a steadily increasing population [26]. He describes the drive for perpetual growth of national economies as “insane”, indicating that there “are simply not enough resources”. In the process he indicates that we are already living beyond the natural regenerative capacities of the biosphere. He proffers that corporate and national economies must be based on sustainability, not the paradigm of unlimited population growth, or the unfettered exploitation of Earth’s resources, continuing that humanity cannot simply reject and change who we are. He indicates that such behavioral changes and expectations must come from a fundamentally different set of awarenesses and practices in our relationships with all the valuables of Earth as they support human life. At the same time, he cautions that “greening” requires global actions and accountability with the same standards being applied to the developed and emerging nations [26].

Value-neutral science, which shuns the contemporary moral and spiritual issues of the delicacy of the current priorities for humanity and its relationship to Earth, represents obsolete thinking [26]. Innovative strategies for science and technology are evolving rapidly with the impacts of artificial intelligence, co-robotics, machine learning, and resilience [25]. These are core activities to be fully incorporated into an integrated vision for diversified natural product research towards replacement medicinal and biological agents, as embraced by the complex term “cyberecoethnopharmacolomics” (CEEPO) [98,99,127], coupled with the initial focus on putting the benefit for the patient (i.e., humanity) first [25,98,99]. AI-prioritized programs must be infused, fostered, and justified based on ethical standards of ecological assessment, sustainability, human values, and accountability, while carefully reflecting on the potential effects of a profitable product with regenerative or reusable potential (beyond biodegradability). Natural products already have several advantages in this regard. The research and development programs of the future to resolve the perennial needs for Medicines Security must reflect compassion for Gaia and no longer abuse our deeply entangled, endangered and vulnerable web. These fundamental attributes of critical thinking about the role of natural products in society should be imbued in all science and technology education programs, not just those exploring Earth for new “valuables”.

6.6 Degrowth and beyond

The various components of the complex term “cyberecoethnopharmacolomics” have been discussed [98,99,127]. One of the “omics” which remains to be briefly presented is the perspective of macroeconomics and its impact on sustainable natural products development for society. Medicines Security relies on a continuously available ecosystem that is not threatened by the local or global macroeconomic environment. Essentially, can an annually increasing GDP co-exist with sustainability and the newly proposed SDGs for 2050? And where does the rapidly emerging concept of "degrowth" in a society (*vide infra*) fit in the panoply of sustainability and "sustainable development"?

In 1848, the English economist and prolific philosopher John Stuart Mill, first published *Principles of Political Economy* in which, over several editions, he developed the concept of a "stationary state", one in which there is zero growth in capital, in financial wealth, and in population [267]. Instead, progress occurs by advancing science and technology through innovation and by improving the well-being (human "development") of the society through mental, moral, and social advancement. This thesis in the contemporary environment clarifies the difference between "growth" and "development". Mill's visionary argument was that continuous economic growth would eventually lead to destruction of the environment and a subsequent lowering of the quality of life. It is remarkable that these ideas were discussed over 170 years ago, when the global population was only about 1.26 billion, and when there were very few concerns regarding the abstraction of assets from the environment for economic growth. Humanity is currently facing the stunning environmental and resource outcomes of ignoring those prognostications from the mid-19th century. The difference for a contemporary Gaia is that those concerns are now very real, are conclusively *not* hypothetical, and must be responded to with great urgency.

As humanity is discovering in the 2020s, in part due to the transition to the more ecocentric 5IR, for ecological longevity societies must shift philosophically and practically from the 4IR and continuous quantitative expansion (growth) to qualitative improvements across diverse economic sectors which minimize, have zero-waste, or do not use, non-renewable resources for their "development". The growth model of a continuously increasing GDP at a 2-3% annual rate can no longer be environmentally and ecologically justified. It is not realistic or sustainable for future generations if non-renewable resources are continuously being depleted without replenishment [1].

The focus for the future must be on cleaning up those sectors that are the most damaging ecologically and socially to avoid continuing the degradation of the ecosystem [81]. GDP-style growth and a net-zero target (impossible by 2030) are antipodal outcomes, especially if any of the projected planetary boundaries [268] are close, or worse, have been exceeded [269,270]. The continuous growth of a GDP extends the linear model which utilizes more non-renewable natural resources. It does not promote a (bio)circular macroeconomy. GDP must be decoupled from negative ecological and environmental impacts [271,272] and concerned scientists have called for that change for the sake of conserving the environment for our descendants [273]. "Green growth" also is, like "sustainable development", an oxymoron [274]. The threatening global situation is an anthropogenic issue, and its diverse impacts on the natural world, including medicinal plants and other terrestrial bioactive resources, the marine environment, and diminished access to chemicals, are not fixable merely through the applications of technology.

The crucial questions become: For future generations is ecosystem protection or continued profitable economic growth towards the ecosystem boundaries more important? Are the current generations willing to own less to protect the assets for the future [275,276]? Can having less now become the more for those who will follow [81]? All the diverse economic sectors of human and technological activity need to be synchronous in developing a collective vision for optimizing the capacity of the ecosystem for a more vibrant Gaia. That vision will modulate over time as the dynamic interplay of societal macro- and microeconomics and the impact on the environment, including the needed ecological assets, such as the medicinal plants and other chemical assets evolve unpredictably. Corporate profit should be allied with the ecological changes (e.g., loss of biodiversity, coastal erosion and flooding, disease prevalence, etc.) of Earth for the next 15-30 years. Substantial support is needed to monetize philosophical and creative investment in the changes that will eventually maintain the benefits, sustainably, for the consumer/patient [1].

In emerging economies, manufacturing capacity may be enhanced and financial wealth raised as the much-needed transitions towards sustainable economic activities occur. More ecological and environmentally challenging lifestyles will evolve locally as a direct result [277]. Which leads to the caution that a holistic appreciation for the ecological" development" of natural products in society is necessary for the future, not one simply based on replacement, replenishment, or bioprospecting.

In *Beyond Growth. The Economics of Sustainable Development*, Daly points out that limiting GDP-type development is an anathema to traditional economists, most politicians, and for-profit businesses who do not accept, or choose to ignore, that the economics of continuous growth depletes the materially finite resources, i.e., having resource boundaries, and irreversibly damages the ecosystem and the environment in multiple ways [277]. Counter-arguments are made that human creativity in science and technology will outpace pollution and depletion caused by burning fossil fuels, and that increasing levels of capital can independently replace natural resources [277], that the "way out" of the pending catastrophe can be bought. The fallacy of these posits is apparent when the natural physical resource boundaries and the non-renewable energy to modulate them for society are limited by the larger ecosystem. It is literally impossible for the macroeconomy to assume a greater societal importance (i.e., endless growth) or even parity with the capacity of the ecosystem [278]. It is postulated that, in some eco-sectors, humanity may already be past that (tipping?) point [26].

For the effective application of Medicines Security there is an important time factor to be addressed: the timeline for continued and availability of the declining, non-renewable resources of the surviving ecosystem for the operation of the macroeconomy in terms of scale and distribution now, and relative to future expanding populations. That guesstimated knowledge and analysis will determine a timeframe for the expanded role of natural products and their derivatives as sustainable medicinal and biological agents. Consequently, because those estimates will be local, the perspectives of the "boundaries" relating to the location and volume of the resources and the projected rate of their utilization are critical elements to be established for national and regional natural product research development plans to be effective. Without restraining "growth" the ecosystem will be depleted uncontrollably for several decades, while attempting to replenish and restore barren environments without targeting specific health care needs. In effect, trying to maintain the *status quo* with disappearing resources.

With the overt failure to meet the 1.5ºC air temperature increase goal of the Paris Agreement in 2023 and 2024, swift action by the high-income countries is necessary to reduce excessive non-renewable resource and energy utilization to attempt to limit even more dramatic ecological and environmental breakdown. There is a movement which projects "degrowth" as a possible answer for limiting and reducing the size of the macroeconomy while offering a revitalizing economic approach functioning within the ecosystem [279]. Degrowth, pioneered by Latouche [279], is regarded as "a planned reduction of excess energy and resources to bring the economy back into balance with the living world in a safe, just and equitable way" [81,280,281]. In this scenario, operating primarily in the developed world [281], an economy is based on human well-being, not the endless drive for expanding the economy, profit, and the accumulation of capital [81]. A comparison of degrowth scenarios with those based on the IPCC constructs revealed that the former was likely to be more effective in restricting deleterious environmental outcomes rather than high-energy use-GDP coupled scenarios, even with large renewable energy inputs [45].

The basis of degrowth is not about reducing an aggregate GDP. Some components of "growth" will be necessary, focused on certain sectors, including for the development and optimization of natural products and the associated chemistry to meet replacement, restorative, and replenishment needs on an industrial scale, for example. Degrowth in practice may involve a shorter working week to maintain high employment levels, allow more time for well-being, and more interpersonal care. It can also promote wealth redistribution and reduce societal inequalities, enhance all levels of education, and guarantee broader health care and affordable housing [81]. It would create a substantially more sustainable culture and be less threatening to ecosystem boundaries. Degrowth is not about meagerness. It is about a larger, less focused, broader, richer, and more appreciative life experience with the myriads of partners on Earth known as "nature", as St. Hildegard espoused for humanity back in the 11th century. Our considerations for the future are therefore between "life" and "death". A "life" for everything on the planet known as Gaia through a significantly reduced production of "needs", or the incessant growth of fulfilling "needs". Or depleting the non-renewable resources of the ecosystem towards an inexorable "death" as the respective tipping points are surpassed and going over the E.D.G.E. occurs. **D.E.G.R.O.W.T.H**. can be summarized as one factor in **D**esigning an **E**conomy **G**enerating **R**eal **O**verarching **W**ealth **T**hrough **H**ealing. Healing Gaia as much as possible for the future custodiams of Earth and healing ourselves through a greater focus on well-being.

An extension of degrowth, Regenerative Development, has been presented by Gabel [1] and elements of this approach have been introduced for discussion throughout this text. It focuses beyond the development of a circular economy to building the capacity to avoid the urgent need to solve "problems" as they arise, and to develop a win/win/win culture which involves in-time decision making based on input from all stakeholders, including consumers/patients, government, industry, and the ecological considerations for a future Earth [1]. It anticipates each succeeding generation leaving an enriched Earth, rather than a beleaguered, poorer Earth, for those who will follow to build qualitative growth in active partnership with nature and technology, rather than a quantitative growth pathway which inevitably destroys the ecological support system for humanity, acknowledging "for without it, we cannot survive" [6].

The clarity of Chief Seattle and the biological interpretations of Gaia take us away from the widespread, Judeo-Christian, dualist thinking that "we" are separate from, above, and can somehow control nature, or even be the "stewards" of nature [282]. This antiquated, anthropocentric approach [283] requires an ethical and moral shift to a highly-focused ecocentric approach. Akin with many holistic religious and indigenous groups, "we", the single human species, are integral as a component of Earth and working actively with the other organisms of Earth, and the technological innovations we devise and deploy, to enhance the environment for all living beings within the deeply interconnected web of *all* life, that bis Gaia. Together, humanity must recognize and understand, with reverence, the importance of maintaining the integrity of the web of nature for the effective functioning of the planet. Wilson has described our situation eloquently as "Half-Earth" [8]. Honoring the interconnectedness of the water systems, of the animals, the insects, the plants, the marine life, etc. is critical for survival and prosperity [6]. Restoration of that kinship with nature must be restored if we are to survive and prosper. Taking a resource solely for transactional human enrichment is morally reprehensible without giving back, replenishing, restoring, and attempting to undo the damage already done. It is *we* who are at nature's "beck and call", not the other way round!! Compassionate reciprocity is required for the enormous gifts from nature that we have received over these millennia. The gifts we enjoy today must be maintained for the survival of our descendants tomorrow [5].

7. CONLCUSIONS

Humanity has never been at this place ever before. The anthropogenic devastation of the environment, and the desires for a concerted response, represent innovative, philosophical, practical, and economic territory for the human experience on planet Earth going forward. However, there is no path "less travelled" for us to take. We must create the new pathways for the remaining period of human survival. We recognize that the future of humanity must reflect a deeply distinctive reverence for the interconnectedness of all life on Earth [4]. Consequently, our intentions, our actions, and our inactions for the next 15-20 years are pivotal for the survival of the 9.44 billion people on Earth in 2045 [48], for the fauna and flora, for the marine environment, for the quality of the air that supports the well-being of all life, and for all that follows, in all the interconnected living domains.

The fate of Earth is now in our hands, for we are the only inhabitants of the planet who have the capacity to destroy it or try to rescue it.

Currently, the world is addicted to the growth of the economies of nations while focused on "sustainable development". That, inherently, cannot be a sustainable pathway for future generations without substantial corrections in the way fossil fuel-based products are utilized. Actions are needed to rebalance our relationship with nature before tipping points are overcome. Without those actions, there can be no return. The moment in time for reassessment and possible correction will have passed. The global addiction to "growth" will have to be assuaged, with understanding across the developed world especially, that what is being relinquished is "not for us but for our descendants" that they may have a holistic life of sufficiency and not "want".

Humans and animals get sick and need medicines for prophylaxis and for treatment. As chemical supplies for synthetic medicines diminish in the next 30 years through "transitioning" from fossil fuels for energy, a major paradigm shift for medicines supply must predict accommodate the available resources to maintain and enhance global health with replacement agents. Plant-based and microbially sourced metabolites and preparations are projected to be the dominant long-term solution for medicinal and biological agents for the coming generations [203]. The ability and ingenuity of natural product scientists, medicinal chemists, pharmaceutical and the medicinal plant industries, and government to act cohesively on this reality and make the practical transition from a non-renewable supply chain for medicinal agents to one that is, at a minimum, totally sustainable, hopefully regenerative, is critical.

The pace of that transition to sustainable sourcing will be an important determinant in global healthcare 30 years from now and beyond. These bioprospecting initiatives can only be effective if Earth's resources are potentiated through L.O.V.E., continually optimizing the valuables that remain. As compassionate, creative scientists and technologists, it is essential to envision this evolving scenario as an incredible opportunity for collaborative and integrated, technology-based, sustainable natural products development as reflected in the term cyberecoethnopharmacolomics (CEEPO) [127]. CEEPO embraces the need for collating and analyzing human knowledge regarding plant assets, is fundamentally focused on sustainability, and on scientific, technological, and sociological integration to serve as the basis for medicinal and biological agent discovery, bioprospecting. Optimization of Earth's resources, of necessity, also includes how human disposed "waste", notably biowaste, must be processed for extended use and serve as a foundation for a new chemical industry. Scientific meetings and gatherings must initiate these issues, promote discussions, and bring plans to address the new directions to those in government, industry, and academia who can commit, over an extended period, the necessary resources to ensure that while the opportunity remains, the moment is seized, for the health and well-being of all of Gaia

Acknowledgements

The background to this article was inspired through discussions with colleagues in many institutions across the world. Their thoughts and clarifications have added immeasurably to the ideas expressed herein.

Conflict of Interest

The author indicates that there are no conflicts of interest associated with this presentation.

References

[1] Gabel, M. (2015, Fall/Winter). Regenerative Development: Going beyond sustainability. *Kosmos Journal for Global Transformation*. Retrieved April 27, 2015 from https://www.kosmosjournal.org/article/regenerative-development-going-beyond-sustainability/.

[2] Ripple, W. J., Wolf, C., Gregg, J. W., Rockström, J., Mann, M. E., Oreskes, N., Lenton, T. M., Rahmstorf, S., Newsome, T.M., Xu, C., Svenning, J.-C., Cardoso Pereira, C., Law, B. E., & Crowther, T. W. (2024). The 2024 state of the climate report: Perilous times on planet Earth. *Bioscience. 74*, 812-824.
[3] Ripple, W. J., Wolf, C., Mann, M. E., Rockström, J., Gregg, J. W., Xu, C., Wunderling, N., Perkins-Kirkpatrick, S. E., Schaeffer. R., Broadgate, W. J., Newsome, T. M., Shuckburgh, E., & Gleick. P. H. (2025). The 2025 state of the climate report: a planet on the brink. *Bioscience*. *75*, biaf149.
[4] Lovelock, J. E. (1979). *Gaia. A New Look at Life on Earth*. Oxford, UK: Oxford University Press. pp. 157.
[5] Anonymous. Web of Life letter. (1854). Retrieved April 5, 2025, from https://www.awakin.org/v2/read/view.php?tid=345.
[6] Maddocks, F. (2001). *Hildegard of Bingen: The Woman of Her Age*. New York, NY: Doubleday. pp. 352.
[7] Carson, R. (1962). *Silent Spring*. Boston, MA: Houghton Mifflin Co. pp. 368.
[8] Wilson, E. O. (2016). *Half-Earth. Our Planet's Fight for Life*. New York, NY: Liveright Publishing Co. pp. 258.
[9] Statista. *Fragrances – Worldwide*. (2025). Retrieved April 5, 2025 from Available at: https://www.statista.com/outlook/cmo/beauty-personal-care/fragrances/worldwide.
[10] Newman, D. J. & Cragg, G. M. (2020). Natural products as sources of new drugs over the nearly four decades from 01/1981 to 09/2019. *Journal of Natural Products*. *83*, 770-803.
[11] Nahavandi, S. (2019). Industry 5.0 - A human-centric solution. *Sustainability. 11*, 4371.
[12] Grabowska, S., Saniuk, S. & Gajdzik, B. (2022). Industry 5.0: improving humanization and sustainability of Industry 4.0. *Scientometrics. 127*, 3117-3144.
[13] Rockström, J., Gupta, J., Qin, D., Lade, S. J., Abrams, J. F., Andersen, L. S., Armstrong McKay, D. I., Bai, X. Bala, G. Bunn, S. E., Ciobanu, D., DeClerck, F., Ebi, K., Gifford, L., Gordon, C., Hasan, S., Kanie, N., Lenton, T. M., Loriani, S., (….), & Zhang, X. (2023). Safe and just Earth system boundaries. *Nature*. *619*(7968), 102-111.
[14] Freedman, W. (2018). Resources and Sustainable Development. In *Environmental Science*. Retrieved April 6, 2025 from https://ecampusontario.pressbooks.pub/environmentalscience/chapter/chapter-12-resources-and-sustainable-development/.
[15] Du Pisani, J. A. (2006). Sustainable development – historical roots of the concept. *Environmental Science*. *3*, 83-96.
[16] Brown, K. (2011). Sustainable adaptation: an oxymoron? *Climate and Development. 3*, 21-31.
[17] Barbier, E. B. & Burgess, J. C. (2017). The Sustainable Development Goals and the systems approach to sustainability. *Economics. 11*, 20170028.
[18] Montani, G. (2007). The ecocentric approach to sustainable development. Ecology, economics and politics. *The Federalist. 49*, 25-60.
[19] Stock, T. & Seliger, G. (2016). Opportunities of sustainable manufacturing in Industry 4.0. *Procedia CIRP. 40*, 536-541.
[20] Breque, M., De Nul, L., & Petridis, A. (2021). *Industry 5.0: towards a sustainable, human-centric and resilient European industry*. Luxembourg, LU: European Commission, Directorate-General for Research and Innovation, 46. Retrieved April 6, 2025 from https://op.europa.eu/en/publication-detail/-/publication/468a892a-5097-11eb-b59f-01aa75ed71a1/.
[21] Longo, F., Padovano, A. & Umbrello, S. (2020). Value-oriented and ethical technology engineering in Industry 5.0: A human-centric perspective for the design of the factory of the future. *Applied Science. 10*, 4182.
[22] Burger, B., Maffettone, P. M., Gusev, V. V., Aitchison, C. M., Bai, Y., Wang, X., Li, X., Alston, B. M., Li, B., Clowes, R., Rankin, N., Harris, B., Sprick, R. S., & Cooper, A. I. (2020). A mobile robotic chemist. *Nature. 583*, 237-241.
[23] Dai, T., Vijayakrishnan, S., Szczypiński, F. T., Ayme, J.-F., Simaei, E., Fellowes, T., Clowes, R., Kotopanov, L., Shields, C. E., Zhou, Z., Ward, J. W., & Cooper, A. I. (2024). Autonomous mobile robots for exploratory synthetic chemistry. *Nature. 635*, 890-897.
[24] Felsberger, A. & Reiner, G. (2020). Sustainable Industry 4.0 in production and operations management: a systematic literature review. *Sustainability. 12*, 7982.
[25] Cordell, G. A. (2024). The contemporary nexus of medicines security and bioprospecting – a future perspective for prioritizing the patient. *Natural Products and Bioprospecting*. *14*, 11.
[26] Sivaraksa, S. (2009). *Wisdom of Sustainability. Buddhist Economics for the 21st Century*. Kihei, HI: Koa Books. pp. 99.

[27] De Jong, M. D. T., Harkink, K. M., & Barth, S. (2018). Making green stuff? Effects of corporate greenwashing on consumers. *Journal of Business and Technical Communication. 32*, 77-112.
[28] AKEPA. Greenwashing: 18 recent stand-out examples. Retrieved April 5, 2025 from https://thesustainableagency.com/blog/greenwashing-examples/.
[29] Verfuerth, C., Demski, C. Capstick, S., Whitmarsh, L., & Poortinga, W. (2023). A people-centred approach is needed to meet net zero goals. *Journal of the British Academy. 11*, 97-124.
[30] Booth, A., Jager, A., Faulkner, S. D., Winchester, C., & Shaw S. E. (2023). Pharmaceutical company targets and strategies to address climate change: content analysis of public reports from 20 pharmaceutical companies. *International Journal of Environmental Research and Public Health. 20*, 3206 (2023).
[31] Partee, E. (2022, June 14). The 1977 White House climate memo that should have changed the world. US Presidential Memo predicted climate change. *The Guardian*. Retrieved April 13, 2025 from https://www.theguardian.com/environment/2022/jun/14/1977-us-presidential-memo-predicted-climate-change.
[32] Watts, N., Adger, N., Agnolucci, P., Blackstock, J., Byass, P., Cai, W., Chaytor, S., Cobourn, T., Collins, M., Cooper, A., Cox, P. M., Depledge, J., Drummond, P., Ekins, P., Galaz, V., Grace, D., Graham, H., Grubb, M., Haines, (….), & A. Costello. (2015). Health and climate change: policy responses to protect public health. *The Lancet. 386*, 1861-1914.
[33] Watts, N., Amann, M., Ayeb-Karlsson, S., Belesova, K., Bouley, T., Boykoff, M., Byass, P., Cai, W., Campbell-Lendrum, D., Chambers, J., Cox, P. M., Daly, M., Dasandi, N., Davies, M., Depledge, M., Depoux, A., Dominguez-Salas, P., Drummond, P., Ekins, P., (….), & A. Costello. (2018). The *Lancet* Countdown on health and climate change: From 25 years of inaction to a global transformation for public health. *The Lancet. 391*, 581-630.
[34] Zyrin, V. & Ilinova, A. (2016). Ecology safety technologies of unconventional oil reserves recovery for sustainable oil and gas industry development. *Journal of Ecological Engineering. 17*, 35-40.
[35] Pisani, N., Boekhout, H. D., Heemskerk, E. M., & Takes, F. W. (2025). China's rise as global scientific powerhouse: A trajectory of international collaboration and specialization in high-impact research. *Research Policy*. *54*, 105288.
[36] Fleck, A. (2025). China pulls far ahead in green energy investment. *Statista* June 24, 2025. https://www.statista.com/chart/34682/global-investment-in-renewable-power-and-fuels/?srsltid=AfmBOooWeO0TKqHmgOLm9b0NBwTUti9Z-BXOal_6XEeonBH0K9T9dMlL Accessed on November 6, 2025.
[37] Tan, R., Hua, H., Zhou, S., Yang, Z., Yang, C., Huang, G., Zeng, J., & Zhao. J. (2025). Current landscape of innovative drug development and regulatory support in China. *Signal Transduction and Targeted Therapy*. *10*, 220.
[38] Waskow, D., Srouji, J., Layke, J., Warszawski, N., Swaby, G., Bhandari, P., Alayza, N., Davey, E., van den Berg, R., Díaz, M. J., Czebiniak, R. P., Langer, P., Chakrabarty, S., Burns, D., Cogswell, N., Cogan, D., & Gerholdt, R. (2023, December). Unpacking COP28: Key outcomes from the Dubai climate talks, and what comes next. Washington, DC; World Resources Institute. Retrieved April 7, 2025 from https://www.wri.org/insights/cop28-outcomes-next-steps.
[39] Lassey, K. R. (2007). Livestock methane emission: From the individual grazing animal through national inventories to the global methane cycle. *Agricultural and Forest Meteorology. 142*, 120-132.
[40] Miller, R. G., & Sorrell, S. R. (2014). The future of oil supply. *Philosophical Transactions of the Royal Society. A 372*, 20130179.
[41] Ediger, V. S., & Berk, I. (2023). Future availability of natural gas: Can it support sustainable energy transition? *Resource Policy. 85,* 103824.
[42] Akyener, O. (2016). Azerbaijan gas export potential and related infrastructures for Eu and Tr energy security issues (up to 2050). *Energy Policy Turkey.* 42-51.
[43] Matthews, H. D., & Wynes, S. (2022). Current global efforts are insufficient to limit warming to 1.5ºC. *Science. 376*, 1404-1409.
[44] Clark, M. A., Domingo, N. G. G., Colgan, K., Thakrar, S. K., Tilman, D., Lynch, J., Azevedo, I. L., & Hill, J. D. (2020). Global food system emissions could preclude achieving the 1.5º and 2ºC climate change targets. *Science*. *370*, 705-708.
[45] Keyßer, L. T., & Lenzen, M. (2021). 1.5ºC Degrowth scenarios suggest the need for new mitigation pathways. *Nature Communications. 12*, 2676.

MALAYSIAN NATURAL PRODUCTS SOCIETY

[46] United Nations Environment Programme. (2024). *Emissions Gap Report 2024: No more hot air … please! With a massive gap between rhetoric and reality, countries draft new climate commitments*. New York, NY. pp. 100. Retrieved April 11, 2025. from https://wedocs.unep.org/20.500.11822/46404.
[47] UNEP-WCMC. (2025). Major takeaways from CBD COP16 in Cali and what's next. Retrieved May 5, 2025 from https://www.unep-wcmc.org/en/news/major-takeaways-from-cbd-cop16-in-cali-and-whats-next.
[48] WorldOMeters. (2025). World Population Clock. Retrieved November 7, 2025 from https://www.worldometers.info/world-population/.
[49] Huss, M. (2024). The Alps' iconic glaciers are melting, but there's still time to save the biggest. *Bulletin of the Atomic Scientists*. *80*, 225-229.
[50] Jones, A. G., Marcott, S.A., Shakun, J. D., Lifton, N. A., Gorin, A. L., Hidy, A. J., Zimmerman, S. R. H., Stock, G. M., Kennedy, T. M., Goehring, B. M., & Caffee, M. A. (2025). Glaciers in California's Sierra Nevada are likely disappearing for the first time in the Holocene. *Science Advances*. *11*, LLNL-JRNL-2006519. https://www.osti.gov/pages/servlets/purl/2998152.
[51] Roe, G. H., Baker, M. B., & Herla, F. (2017). Centennial glacier retreats as categorical evidence of regional climate change. *Nature Geoscience. 10*, 95-99.
[52] Milillo, P., Rignot, E., Rizzoli, P., Scheuchl, B., Mouginot, J., Bueso-Bello, J., & Prats-Iraola, P. (2019). Heterogeneous retreat and ice melt of Thwaites Glacier, West Antarctica. *Science Advances. 5*, eaau3433.
[53] Berwyn, B. (2024, September 19), A new science briefing from an international research team can't rule out some of the worst-case sea level rise scenarios, including six feet by 2100. *Inside Climate News*. Retrieved April 7, 2025 from https://insideclimatenews.org/news/19092024/grim-outlook-for-thwaites-glacier/.
[54] Igini, M. (2022, June 9). Sea level rise projections: 10 Cities at risk of flooding. Retrieved April 7, 2025 from https://earth.org/sea-level-rise-projections/.
[55] Larour, E., Ivins, E. R., & Adhikari, S. (2017). Should coastal planners have concern over where land ice is melting? *Science Advances. 3*, e1700537.
[56] Lin, Y., McDermott, T. K. J., & Michaels, G. (2024). Cities and the sea level. *Journal of Urban Economics. 143*, 103685.
[57] Herdiawanto, H. (2023). The position of the Nusantara Capital City from a national security perspective. *Masyarakat, Kebudayaan & Politik. 36*, 545.
[58] Mimura, N. (1999). Vulnerability of island countries in the South Pacific to sea level rise and climate change. *Climate Research*. *12*, 137-143.
[59] Hauer, M. E., Fussell, E., Mueller, V., Burkett, M., Call, M., Abel, K., McLeman, R., & Wrathall, D. (2020). Sea-level rise and human migration. *Nature Reviews Earth and Environment. 1*, 28-39.
[60] Ginsburg, A. (2025, April 7). NYC metro area could lose 80,000 homes to flooding by 2040. Retrieved April 7, 2025 from https://www.6sqft.com/nyc-metro-area-could-lose-80000-homes-to-flooding-by-2040/.
[61] Sayers, P., Moss, C., Carr, S., & Payo, A. (2022). Responding to climate change around England's coast - The scale of the transformational challenge. *Ocean & Coastal Management.* **225**, 106187.
[62] Li, Y., Kong, D., Fu, Y., Sussman, M. R., & Wu, H. (2020). The effect of developmental and environmental factors on secondary metabolites in medicinal plants. *Plant Physiology and Biochemistry. 148*, 80-89.
[63] Pant, P., Pandey, S., & Dall'Acqua, S. (2021). The influence of environmental conditions on secondary metabolites in medicinal plants: A literature review. *Chemistry and Biodiversity. 18*, e2100345.
[64] Munir, N., Hasnain, M., Roessner, U., & Abideen, Z. (2022). Strategies in improving plant salinity resistance and use of salinity resistant plants for economic sustainability. *Critical Reviews in Environmental Science and Technology. 52*, 2150-2196.
[65] Rastogi, S., Shah, S., Kumar, R., Vashisth, D., Akhtar, Md. Q., Kumar, A., Dwivedi, U.N., & Shasany, A. K. (2019). *Ocimum* metabolomics in response to abiotic stresses: Cold, flood, drought and salinity. *PloS One. 14*, e0210903.
[66] Golkar, P., Taghizadeh, M., & Yousefian, Z. (2019). The effects of chitosan and salicylic acid on elicitation of secondary metabolites and antioxidant activity of safflower under *in vitro* salinity stress. *Plant Cell, Tissue and Organ. Culture*. *137*, 575-585.
[67] Bistgani, Z. E., Hashemi, M., DaCosta, M., Craker, L., Maggi, F., & Morshedloo, Md. R. (2019). Effect of salinity stress on the physiological characteristics, phenolic compounds and antioxidant activity of *Thymus vulgaris* L. and *Thymus daenensis* Celak. *Industrial Crops and Products. 135*, 311-320.

[67] Saleem, A., Anwar, S., Nawaz, T., Fahad, S., Saud, S., Ur Rahman, T., Khan, M. N. R., & Nawaz, T. (2025). Securing a sustainable future: the climate change threat to agriculture, food security, and sustainable development goals. *Journal of Umm Al-Qura University for Applied Sciences*. *11*, 595-611.
[69] Mofokeng, M. M., Du Plooy, C. P., Araya, H. T., Amoo, S. O., Mokgehle, S. N., Pofu, K. M., & Mashela, P. W. (2022). Medicinal plant cultivation for sustainable use and commercialisation of high-value crops. *South African Journal of Science*. *118*, 1-7.
[70] Perkins-Kirkpatrick, S. E., Palmer, L., King, A., & Ziehn. T. (2025). Heatwaves in a net zero World. *Environmental Research: Climate.* Accepted online. doi 10.1088/2752-5295/ae0ea4.
[71] Intergovernmental Panel on Climate Change. (2018). *Special Report: Climate Change and Land*. Retrieved April 21, 2025 from https://www.ipcc.ch/site/assets/uploads/2018/07/sr2_background_report_final.pdf.
[72] Mohamed, A. A., Omar, I. M., Ibey, A. M. Y., & Omar, M. M. (2025). Climate change and migration dynamics in Somalia: a time series analysis of environmental displacement. *Frontiers in Climate*. *6*, 1529420.
[73] Oxford Analytica. Both growth and hardship set to endure in Guatemala. *Daily Briefing*. Dec 16 2022. https://doi.org/10.1108/OXAN-DB274741. Accessed November 6, 2025.
[74] Liebelt, D. J., Jordan, J. T., & Doherty, C. J. (2019). Only a matter of time: The impact of daily and seasonal rhythms on phytochemicals. *Phytochemistry Reviews. 18*, 1409-1433.
[75] Ma, D.-M., Gandra, S. V. S., Manoharlal, R., La Hovary, C., & Xie, D.-Y. (2019). Untargeted metabolomics of *Nicotiana tabacum* grown in United States and India characterizes the association of plant metabolomes with natural climate and geography. *Frontiers in Plant Science. 10*, 1370.
[76] Xu, W., Cheng, Y., Guo, Y., Yao, W., & Qian, H. (2022). Effects of geographical location and environmental factors on metabolite content and immune activity of *Echinacea purpurea* in China based on metabolomics analysis. *Industrial Crops and Products. 189*, 115782.
[77] Patni, B., Bhattacharyya, M., Kumari, A., & Purohit, V. K. (2022). Alarming influence of climate change and compromising quality of medicinal plants. *Plant Physiology Reports.* ***27***, 1-10.
[78] Mehalaine, S., & Chenchouni, H. (2021). Quantifying how climatic factors influence essential oil yield in wild-growing plants. *Arabian Journal of Geosciences. 14*, 1257.
[79] United Nations World Meteorological Office. (2025, March). *State of the Climate 2024*. Retrieved April 5, 2025 from https://wmo.int/publication-series/state-of-global-climate-2024.
[80] Steffen, W., Rockström, J., Richardson, K., Lenton, T. M., Folke, C., Liverman, D., Summerhayes, C. P., Barnosky, A. D., Cornell, S. E., Crucifix, M., Donges, J. F., Fetzer, I., Lade, S. J., Schefer, M., Winkelmann, R., & Schnellmhuber, H. J. (2018). Trajectories of the Earth system in the Anthropocene. *Proceedings of the National Academy of Sciences, United States of America*. *115*, 8252-8259.
[81] Hickel, J. (2022). *Less is More. How Degrowth will Save the World*. Dublin, Ireland, Penguin Books. pp. 320.
[82] North, A. (2023, November 27). You can't even pay people to have more kids. Retrieved April 7, 2025 from https://www.vox.com/23971366/declining-birth-rate-fertility-babies-children.
[83] Breinlinger, S., Phillips, T. J., Haram, B. N., Mareš, J., Martínez Yerena, J. A., Hrouzek, P., Sobotka, R., Henderson, W. M., Schmieder, P., Williams, S. M., Lauderdale, J. D., Wilde, H.D., Gerrin, W., Kust, A., Washington, J. W., Wagner, C., Geier, B., Liebeke, M., Enke, H., Niedermeyer, T. J., & Wilde, S. B. (2021). Hunting the eagle killer: A cyanobacterial neurotoxin causes vacuolar myelinopathy. *Science*. *371*, eaax9050.
[84] Kehoe, R., Frago, E., & Sanders, D. (2021). Cascading extinctions as a hidden driver of insect decline. *Ecological Entomolology*. *46*, 743-756.
[85] Smith, E. (2024, September 25). Project Guacamaya uses daily satellite images, Amazon-specific AI models in battle against deforestation. *LATAM Magazine*. Retrieved April 7, 2025 from https://news.microsoft.com/source/latam/features/ai/project-guacamaya-rainforest-deforestation/?lang=en.
[86] Lapola, D. M., Pinho, P., Barlow, J., Aragão, L. E. O. C., Berenguer, E., Carmenta, R., Liddy, H. M., Seixos, H., Silva, C. V. J., Silva-Funior, C. H. L., Alencar, A. A. C., Anderson, L. O., Armenteras, D., Brovkin, V., Calders, K., Chambers, J., Chini, L., Costa, M. H., Faria, B. L., (….), & Walker, W. S. (2023). The drivers and impacts of Amazon forest degradation. *Science. 379*, 349.
[87] Thurstan, R. H., Brockington, S., & Roberts, C. M. (2010). The effects of 118 years of industrial fishing on UK bottom trawl fisheries. *Nature Communications*. *1*, 15.
[88] FAO. (2024). *The State of World Fisheries and Aquaculture. Blue Transformation in Action*. Rome, Italy. pp. 264.

[89] Althaus, F., Williams, A., Schlacher, T. A., Kloser, R. J., Green, M. A., Barker, B. A., Bax, N. J., Brodie, P., & Schlacher-Hoenlinger, M. A. (2009). Impacts of bottom trawling on deep-coral ecosystems of seamounts are long-lasting. *Marine Ecology - Progress Series. 397*, 279-294.
[90] Coral Reef Watch. (2025, April 21). National Oceanic and Atmospheric Administration. Current Global Bleaching: Status Update & Data Submission. Retrieved April 25, 2025 from https://www.coralreefwatch.noaa.gov/satellite/research/coral_bleaching_report.php.
[91] Lenton, T. M., Milkoreit, M., Willcock, S., Abrams, J.F., Armstrong McKay, D.I., Buxton, J.E., Donges, J.F., Loriani, S., Wunderling, N., Alkemade, F., Barrett, M., Constantino, S., Powell, T., Smith, S.R., Boulton, C. A., Pinho, P., Dijkstra, H.A. Pearce-Kelly, P., Roman- Cuesta, R.M., Dennis, D. (eds), (2025). The Global Tipping Points Report 2025. pp. 379. Available at https://global-tipping-points.org/ Accessed October 14, 2025.
[92] Bajaj, P. (2020). On oceans and climate change. *Maritime* 9.
[93] Klein, S. G., Roch, C., & Duarte, C. M. (2024). Systematic review of the uncertainty of coral reef futures under climate change. *Nature Communications*. *15*, 2224.
[94] Pinsky, M. L., Eikeset, A. M., McCauley, D. J., Payne, J. L., & Sunday, J. M. (2019). Greater vulnerability to warming of marine versus terrestrial ectotherms. *Nature. 569*, 108-111.
[95] De Vos, J. M., Joppa, L. N., Gittleman, J. L., Stephens, P. R., & Pimm, S.L. (2015). Estimating the normal background rate of species extinction. *Conservation Biology. 29*, 452-462.
[96] Ceballos, G., Ehrlich, P. R., & Dirzo, R. (2017). Biological annihilation via the ongoing sixth mass extinction signaled by vertebrate population losses and declines. *Proceedings of the National Academy of Sciences, United States of America*. *114*, E6089-E6096.
[97] Antonelli, A. and collaborators. (2023). *State of the World's Plants and Fungi 2023*. Richmond, UK: Royal Botanic Gardens Kew, UK. Retrieved April 7, 2015 from https://doi.org/10.34885/wnwn-6s63.
[98] Cordell, G. A. (2017). Sixty challenges – a 2030 perspective on natural products and medicines security. *Natural Product Communications*. *12*, 1371-1379.
[99] Daley, S.-k., & Cordell, G. A. (2021). Natural products, the fourth industrial revolution and the quintuple helix. *Natural Product Communications*. *16*, 1-31.
[100] Farnsworth, N. R., Akerele, O., Bingel, A. S., Soejarto, D. D., & Guo, Z. (1985). Medicinal plants in therapy. *Bulletin of the World Health Organization. 63*, 965-981.
[101] Picking, D., Younger, N., Mitchell, S., & Delgoda, R. (2011). The prevalence of herbal medicine home use and concomitant use with pharmaceutical medicines in Jamaica. *Journal of Ethnopharmacology. 137*, 305-311.
[102] United Nations General Assembly. (1987, August 4). *Report of the World Commission on Environment and Development: Our Common Future*. An annex to document A/42/427. Retrieved May 6, 2025 from https://digitallibrary.un.org/record/139811?ln=en&v=pdf.
[103] *Keeble, B. R. (1988). The Brundtland Report: 'Our Common Future'. Medicine and War. 4,* 17-25. doi:10.1080/07488008808408783
[104] Meadows, D. H., Meadows, D. L., Randers, J., & Behrens, III, W.W. (1972). *The Limits to Growth; A Report for the Club of Rome's Project on the Predicament of Mankind.* New York, NY: Universe Books. Retrieved April 7, 2025 from https://www.clubofrome.org/publication/the-limits-to-growth/
[105] Meadows, D., Randers, J., & Meadows, D. (2004). *Limits to Growth: The 30-Year Update*. White River Junction, VT: Chelsea Green Publishing Co. pp. 370.
[106] Turner, G. (2008), A comparison of 'The Limits to Growth' with thirty years of reality. *Global Environmental Change*. *18*, 397-411.
[107] Hall, C. A. S., & Day, J. W. (2009). Revisiting the Limits to Growth after peak oil. *American Scientist. 97*, 230-237.
[108} Nebel, A., Kling, A., Willamowski, R., & Schell, T. (2023). Recalibration of Limits to Growth: an update of the World3 model. *Journal of Industrial Ecology*. *28*, 87-99.
[109] International Union for Conservation of Nature and Natural Resources. (1980). *World Conservation Strategy: Living Resource Conservation for Sustainable Development.* Retrieved April 7, 2025 from https://portals.iucn.org/library/efiles/documents/WCs-004.pdf.
[110] Haines, A., & Cassels, A. (2004). Can the Millennium Development Goals be attained? *British Medical Journal. 329*, 394-397.
[111] de Jong, E., & Vijge, M. J. From Millennium to Sustainable Development Goals: evolving discourses and their reflection in policy coherence for development. *Earth System Governance.* **7**, 100087.

[112] Hulme, D., & Scott, J. (2010). The political economy of the MDGs : Retrospect and prospect for the world's biggest promise. Manchester: University of Manchester. Brooks World Poverty Institute.
[113] Sachs, J.D. (2015). *The Age of Sustainable Development*. New York, NY, USA, Columbia University Press.
[114] UNESCO. (2015). Sustainable development. Retrieved March 15, 2015 from https://www.unesco.org/en/sustainable-development.
[115] Robert, K. W., Parris, T. M., & Leiserowitz, A. A. (2005). What is sustainable development? Goals, indicators, values, and practice. *Environment: Science and Policy for Sustainable Development*. *47*, 8-21.
[116] Mensah, J. (2019). Sustainable development: meaning, history, principles, pillars, and implications for human action: literature review. *Cogent Social Sciences*. *5*, 1653531.
[117] Purvis, B., Mao, Y., & Robinson, D. (2019). Three pillars of sustainability: in search of conceptual origins. *Sustainability Science. 14*, 681-695.
[118] William, C. C., & Millington, A. C. (2004). The diverse and contested meanings of sustainable development. *Geographical Journal*. *170*, 99-104.
[119] Yunita, A., Biermann, F., Kim, R. E., & Vijge, M. J. (2022). The (anti-)politics of policy coherence for sustainable development in the Netherlands: logic, methods, effects. *Geoforum. 128*, 92-102.
[120] Ramsey, J. L. (2015). On not defining sustainability. *Journal of Agricultural and Environmental Ethics. 28*, 1075-1087.
[121] International Resource Panel. (2011). Decoupling natural resource use and environmental impacts from economic growth. Nairobi, Kenya; United Nations Environmental Programme. Available at: https://www.unep.org/resources/report/decoupling-natural-resource-use-and-environmental-impacts-economic-growth.
[122] Scheel, C., Aguiñaga, E., & Bellom B. (2020). Decoupling economic development from the consumption of finite resources using circular economy. A model for developing countries. *Sustainability. 12*, 1291.
[123] Tichy, G. (2023, May). The 17 SDG goals and their 169 targets. Retrieved March 31, 2015 from https://www.stratecta.exchange/the-17-sdg-goals-and-their-169-targets/.
[124] Anonymous. (2024). SDGs – finding a balance between attainability and urgency. *Nature. 630*, 529.
[125] Nerini, F. F., Mazzucato, M., Rockström, J., van Asselt, H., Hall, J. W., Matos, S., Persson, Å., Sovacool, B., Vinuesa, R., & Sachs, J. (2024). Extending the Sustainability Development Goals to 2050 – a road map. *Nature. 630*, 555-558.
[126] United Nations. (2024). *Pact for the Future. Global Digital Compact. Declaration on Future Generations.* New York, NY: United Nations. Retrieved April 9, 2025 from https://www.un.org/sites/un2.un.org/files/sotf-pact_for_the_future_adopted.pdf.
[127] Cordell, G. A. (2019). Cyberecoethnopharmacolomics. *Journal of Ethnopharmacology*. *244*, 112134.
[128] Berg, C. (2019). *Sustainable Action: Overcoming the Barriers*. Abingdon, UK: Routledge. pp. 318.
[129] Howes, M., Wortley, L., Potts, R., Dedekorkut-Howes, A., Serrao-Neumann, S., Davidson, J., Smith, T., & Nunn, P. (2017). Environmental sustainability: a case of policy implementation failure. *Sustainability. 9*, 165.
[130] Harrington, L. M. B. (2016). Sustainability theory and conceptual considerations: A review of key ideas for sustainability and the rural context. *Papers in Applied Geography*. *2*, 365-382.
[131] Dahlhaus N. & Weißkopf, D. (2017). *Future Scenarios of Global Cooperation - Practices and Challenges. Global Dialogs 14.* (pp. 11-23). Duisberg, Germany: Centre for Global Cooperation Research.
[132] Wiedmann, T., Lenzen, M., Keyßer, L.T., & Steinberger, J. K. (2020). Scientists' warning on affluence. *Nature Communications*. *11*, 3107.
[133] World Business Council for Sustainable Development. (2021). *Vision 2050 – Time to Transform*. Geneva, Switzerland. Retrieved May 6, 2025 from https://www.wbcsd.org/vision-2050/.
[134] International Health Conference. (2002). Constitution of the World Health Organization, 1946. *Bulletin of the World Health Organization*. *80*, 983-998.
[135] Schmidhuber, J., & Tubiello, F. N. (2007). Global food security under climate change *Proceedings of the National Academy of Sciences, United States of America. 104*, 19703-19708.
[136] Wheeler, T., & von Braun, J. (2013). Climate change impacts on global food security. *Science. 341*, 508-513.
[137] Muluneh, M. (2021). Impact of climate change on biodiversity and food security: a global perspective - a review article. *Agriculture and Food Security. 10*, 1-25.

[138] Mirzabaev, A., Kerr, R.B., Hasegawa, T., Pradhan, P., Wreford, A., von der Pahlen, M. C. T., & Gurney-Smith, H. (2023). Severe climate change risks to food security and nutrition. *Climate Risk Management. 39*, 100473.
[139] World Health Organization. (2002). WHO Traditional Medicine Strategy 2002–2005. Geneva, Switzerland: World Health Organization. Retrieved April 9, 2025 from https://www.who.int/publications/i/item/WHO-EDM-TRM-2002.1.
[140] World Health Organization. (2013). WHO Traditional Medicine Strategy: 2014-2023. Geneva, Switzerland: World Health Organization. Retrieved April 9, 2025 from https://iris.who.int/handle/10665/92455.
[141] World Health Organization. (2024). Draft global traditional medicine strategy (2025–2034). Geneva, Switzerland: World Health Organization. Retrieved April 9, 2025 from https://apps.who.int/gb/ebwha/pdf_files/EB156/B156_16-en.pdf.
[142] Anonymous. (2008). WHO congress backs traditional medicine. *Nature. 456*, 152.
[143] World Health Organization. (2017 November). 1 in 10 medical products in developing countries is substandard or falsified. Retrieved April 12, 2025 from https://www.who.int/news/item/28-11-2017-1-in-10-medical-products-in-developing-countries-is-substandard-or-falsified.
[144] McMichael, A. J., Woodruff, R. E., & Hales, S. (2006). Climate change and human health: present and future risks. *The Lancet. 367*, 859-869.
[145] Patz, J. A., Campbell-Lendrum, D., Holloway, T., & Foley, J. A. (2005). Impact of regional climate change on human health. *Nature. 438*, 310-317.
[146] GBD 2021 Forecasting Collaborators. (2024). Burden of disease scenarios for 204 countries and territories, 2022-2050: a forecasting analysis for the Global Burden of Disease Study 2021. *The Lancet. 403*, 2204-2256.
[147] IQVIA Institute for Human Data Science. (2024). *Global Use of Medicines: Outlook to 2028*. NJ, USA, Parsippany. pp. 58. Available from www.iqviainstitute.org.
[148] Nath, R., Kityania, S., Nath, D., Das Talkudar, A., & Sarma, G. (2023). An extensive review on medicinal plants in the special context of economic importance. *Asian Journal of Pharmaceutical and Clinical Research. 16*, 6-11.
[149] Willison, K. D., & Andrews, G.J. (2004). Complementary medicine and older people: Past research and future directions. *Complementary Therapies in Nursing and Midwifery.* **10**, 80-91.
[150] Saklani, A., & Kutty, S. K. (2008). Plant-derived compounds in clinical trials. *Drug Discovery Today. 13*, 161-171.
[151] Verma, S., & Singh, S. (2008). Current and future status of herbal medicines. *Veterinary World.* 2, 347.
[152] Hoareau, L., & DaSilva, E. J. (1999). Medicinal plants: A re-emerging health aid. *Electronic Journal of Biotechnology*. *2*, 3-4.
[153] Briskin, D. P. (2000). Medicinal plants and phytomedicines. Linking plant biochemistry and physiology to human health. *Plant Physiology*. *124*, 507-514.
[154] Khan, H. (2014). Medicinal plants in light of history: Recognized therapeutic modality. *Journal of Evidence-Based Complementary and Alternative Medicine*. *19*, 216-219.
[155] Beyene, B., Beyene, B., & Deribe, H. (2016). Review on application and management of medicinal plants for the livelihood of the local community. *Journal of Resources Development and Management*. *22,* 33-39.
[156] Vaidya, A. D., & Devasagayam, T. P. (2007). Current status of herbal drugs in India: An overview. *Journal of Clinical Biochemistry and Nutrition*. *41*, 1-11.
[157] Tangjitman, K., Trisonthi, C., Wongsawad, C., Jitaree, S., & Svenning, J. C. (2015). Potential impact of climatic change on medicinal plants used in the Karen women's health care in Northern Thailand. *Songklanakarin Journal of Science and Technology*. *37*, 369-379.
[158] Yi, Y., Cheng, X., Yang, Z., & Zhang, S. (2016). Maxent modeling for predicting the potential distribution of endangered medicinal plant (*H. riparia* Lour.) in Yunnan, China. *Ecological Engineering*. *92*, 260-269.
[159] Wei, B., Wang, R. Hou, K., Wang, X., & Wu, W. (2018). Predicting the current and future cultivation regions of *Carthamus tinctorius* L. using MaxEnt model under climate change in China. *Global Ecology and Conservation*. *16*, e00477 (2018).
[160] Khanum, R., Mumtaz, A. S., & Kumar, S. (2013). Predicting impacts of climate change on medicinal asclepiads of Pakistan using Maxent modeling. *Acta Oecologica*. *49*, 23-31.

[161] Asase, A., & Peterson, A. T. (2019). Predicted impacts of global climate change on the geographic distribution of an invaluable African medicinal plant resource, *Alstonia boonei* De Wild. *Journal of Applied Research on Medicinal and Aromatic Plants. 14*, 100206.
[162] Tshabalala, T., Mutanga, O., & Abdel-Rahman, E. M. (2022). Predicting the geographical distribution shift of medicinal plants in South Africa due to climate change. *Conservation. 2*, 694-708.
[163] Gairola, S., Shariff, N. Mohd., Bhatt, A., & Kala, C. P. (2010). Influence of climate change on production of secondary chemicals in high altitude medicinal plants: Issues need immediate attention. *Journal of Medicinal Plants Research. 4*, 1825-1829.
[164] Manish, K. (2022). Medicinal plants in peril due to climate change in the Himalaya. *Ecological Informatics. 68*,101546.
[165] Cavaliere, C. (2009). The effects of climate change on medicinal and aromatic plants. *Herbalgram. 81*, 44-57.
[166] Harish, B. S., Dandin, S. B., Umesha, K., & Sasanur, A. (2012). Impact of climate change on medicinal plants - a review. *Ancient Science of Life. 32*, Suppl. 1, S23.
[167] Das, M., Jain, V., & Malhotra, S. K. (2016). Impact of climate change on medicinal and aromatic plants. *Indian Journal of Agricultural Sciences. 86*, 1375-1382.
[168] Gupta, A., Singh, P. P., Singh, P., Singh, K., Singh, A. V., Singh, S. K., & Kumar, A. (2019). Medicinal plants under climate change: impacts on pharmaceutical properties of plants. In *Climate Change and Agricultural Ecosystems*. New Delhi, India; Woodhead Publishing.
[169] Patni, B., Bhattacharyya, M., Kumari, A., & Purohit, V. K. (2022). Alarming influence of climate change and compromising quality of medicinal plants. *Plant Physiology Reports. 27*, 1-10).
[170] Hounsou, E. K., Sonibare, M. A., & Elufioyem T. O. (2024). Climate change and the future of medicinal plants research. *Bioactive Compounds in Health and Disease. 7*, 152-169.
[171] Applequist, W. L., Brinckmann, J. A., Cunningham, A. B., Hart, R. E., Heinrich, M., Katerere, D. R., & Van Andel, T. (2020). Scientists' warning on climate change and medicinal plants. *Planta Medica. 86*, 10-18.
[172] Cahyaningsih, R., Phillips, J., Magos Brehm, J., Gaisberger, H., & Maxted, N. (2021). Climate change impact on medicinal plants in Indonesia. *Global Ecology and Conservation. 30*, e01752.
[173] Mofokeng, M. M., Du Plooy, C. P., Araya, H. T., Amoo, S. O., Mokgehle, S. N., Pofu, K. M., & Mashela, P. W. (2022). Medicinal plant cultivation for sustainable use and commercialisation of high-value crops. *South African Journal of Science. 118*, 1-7.
[174] Ezeako, E. C., Solomon, A. Y., Itam, Y. B., Ezike, T., Ogbonna, C. P., Amuzie, N. G., Aham, E. C., Aondover, C. D., Osuagwu, G. O. & Ozougwu, V. E. (2025). Prospects of synthetic biology in revolutionizing microbial synthesis and drug discovery. *Life Research*. *8*, 6-15.
[175] Ahmad, M., Tahir, M., Hong, Z., Zia, M. A., Rafeeq, H., Ahmad, M. S., ur Rehman, S., & Sun, J. (2025). Plant and marine-derived natural products: sustainable pathways for future drug discovery and therapeutic development. *Frontiers in Pharmacology*. *15*, 1497668.
[176] dos Santos Silva, I., Soares, L., & Schifferdecker-Hoch, F. (2024). 7 Dimensions of holistic wellbeing (7DHW): a theoretical model. *Archives of Internal Medicine Research*. *7*, 321-330.
[177] Cordell, G. A., & Colvard, M. D. (2007). Natural products in a world out-of-balance. *Arkivoc*, *vii*, 97-115.
[178] Azevedo, G., & Gates, A. (2019). Wake up! The world is out of balance and if you do nothing you are part of the problem: An interview with Henry Mintzberg. *Journal of Management Inquiry. 28*, 180-186.
[179] Madan, G., Gjermundsen, A., Iversen, S. C., & LaCasce, J. H. (2024). The weakening AMOC under extreme climate change. *Climate Dynamics*. *62*, 1291-1309.
[180] Muttitt, G. & Kartha, S. (2020). Equity, climate justice and fossil fuel extraction: principles for a managed phase out. *Climate Policy*. *20*, 1024-1042.
[181] Koplan, A. P., Bond, T. C., Merson, M. H., Reddy, K. S., Rodriguez, M. H., Sewankambo, N. K., & Wasserheit, J. N. (2009). Towards a common definition of global health. *The Lancet. 373*, 1993-1995.
[182] J. Tollefson. Coral die-off marks Earth's first climate 'tipping point', scientists say. *Nature*. Oct. 12, 2025. Accessed on November 7, 2025 at https://www.nature.com/articles/d41586-025-03316-w.
[183] Gore, A., & Guggenheim, D. (2008, May). *An Inconvenient Truth*. Paramount Classics.
[184] United States Food and Drug Administration. (2025). Drug shortages. Retrieved April 11, 2025 from https://www.fda.gov/drugs/drug-safety-and-availability/drug-shortages.

[185] Reibel, J. B., Sun, L. L., Parikh, R. B., Mahmud, N., Martin, L. P., Hubbard, R. A., & Mamtani, R. (2024). Real-world impact of the platinum chemotherapy shortage on US patients with advanced cancer. *Journal of the National Cancer Institute.* djae307 (2024).
[186] US Food and Drug Administration. Recalls, Market Withdrawals, & Safety Alerts. https://www.fda.gov/safety/recalls-market-withdrawals-safety-alerts. Accessed on November 6, 2025.
[187] Cordell, G. A. (2014). Phytochemistry and traditional medicine – the revolution continues. *Phytochemistry Letters*. *10*, 28-40.
[188] Cordell, G. A. (2015). Ecopharmacognosy - the responsibilities of natural product research to sustainability. *Phytochemistry Letters*. *11*, 332-346.
[189] Cordell, G. A. (2015). Alice, benzene, and coffee: the ABC's of ecopharmacognosy. *Natural Products Communications*. *10*, 2195-2202.
[190] Cohen, P. A., Avula, B., Wang, Y.-H., Katragunta, K., & Khan, I. (2023). Quantity of melatonin and CBD in melatonin gummies sold in the US. *Journal of the American Medical Association. 329*, 1401-1402.
[191] Ichim, M. C. (2019). The DNA-based authentication of commercial herbal products reveals their globally widespread adulteration. *Frontiers in Pharmacology*. *10*, 1227.
[192] Ichim, M. C., & Booker, A. (2021). Chemical authentication of botanical ingredients: a review of commercial herbal products. *Frontiers in Pharmacology. 12*, 666850.
[193] Cordell, G. A. (2018). Ecopharmacognosy - why natural products matter - now and for the future. *Thai Bulletin of Pharmaceutical Sciences*, *13*, 1-9.
[194] Martirosyan D. & Saharsh T. (2025). The science, safety, and policy of dietary supplements: A comprehensive review and future roadmap. *Dietary Supplements and Nutraceuticals*. *4*, 25-36.
[195] Deming, W. E. (1982). *Out of the Crisis*. Cambridge, MA: MIT Press. pp. 672.
[196] Guo, D.-a., Wu, W.-Y., Ye, M., Liu, X., & Cordell, G. A. (2015). A holistic approach to the quality control of traditional Chinese medicines. *Science. 347*, S29-31.
[197]. Daley, S.-k. & Cordell, G. A. (2021). Alkaloids in contemporary drug discovery to meet global disease needs. *Molecules*. *26*, 03800.
[198] World Health Organization, WHO Model List of Essential Medicines. 23rd List. World Health Organization, Geneva, Switzerland, 2023, 71 pp. Available at: https://www.who.int/publications/i/item/WHO-MHP-HPS-EML-2023.02.
[199] Yegros-Yegros, A., van de Klippe, W., Abad-Garcia, M. F., & Rafols, I. (2020). Exploring why global health needs are unmet by research efforts: the potential influences of geography, industry and publication incentives. *Health Research Policy and Systems. 18*, 47.
[200] Chu, H., Zhang, A.-H., Han, Y., & Wang, X.-J. (2015). Metabolomics and its potential in drug discovery and development from TCM. *World Journal of Traditional Chinese Medicine. 1*, 26-32.
[201] Salem, M. A., de Souza, L. P., Serag, A., Fernie, A. R., Farag, M. A., Ezzat, S. M., & Alseekh, S. (2020). Metabolomics in the context of plant natural products research: From sample preparation to metabolite analysis. *Metabolites. 10*, 37.
[202] Simoben, C. V., Babiaka, S. B., Moumbock, A. F. A., Namba-Nzanguim, C. T., Eni, D. B., Medina-Franco, J. L., Günther, S., Ntie-Kang, F., & Sippl, W. (2023). Challenges in natural product-based drug discovery assisted with *in silico*-based methods. *RSC Advances*. *13*, 31578-31594.
[203] Cordell, G. A. (2011, June 27). Plant medicines - key to global health. *Chemical and Engineering News.* 52-56.
[204] Cordell, G. A., Lemos, T. L. G., Monte, F. J. Q., & de Mattos, M C. (2007). Vegetables as chemical reagents. *Journal of Natural Products*. *70*, 478-492.
[205] Srirama, R., Kumar, J. U. S., Seethapathy, G. S., Newmaster, S. G., Ragupathy, S., Ganeshaiah, K. N., Shaanker, R. U., & Ravikanth, G. (2017). Species adulteration in the herbal trade: causes, consequences and mitigation. *Drug Safety. 40*, 651-661.
[206] Luo, Y., Yang, H., & Tao, G. (2024). Systematic review on fingerprinting development to determine adulteration of Chinese herbal medicines. *Phytomedicine. 129*, 155667.
[207] Gaffner, S., Loffredo, L., Kababick, J., Wise, S. M., & Upton, R. (2024). The undisclosed presence of excipients and diluents in botanical extracts. *Herbalgram. 140*, 44-50.

[208] Czigle, S., Tóth, J., Jedlinszki, N., Háznagy-Radnai, E., Csupor, D., & Tekeľová, D. (2018). *Ginkgo biloba* food supplements on the European market – adulteration patterns revealed by quality control of selected samples. *Planta Medica*. *84*, 475-482.
[209] Collins, B. J., Kerns, S. P., Aillon, K., Mueller, G., Rider, C. V., DeRose, E. F., London, R. F., Harnly, J. M. & Waidyanatha, S. (2020). Comparison of phytochemical composition of *Ginkgo biloba* extracts using a combination of non-targeted and targeted analytical approaches. *Analytical and Bioanalytical Chemistry*. *412*, 6789-6809.
[210] Booker, A., Frommenwiler, D., Reich, E., Horsfield, S., & Heinrich, M. (2016). Adulteration and poor quality of *Ginkgo biloba* supplements. *Journal of Herbal Medicine*. *6*, 79-87.
[211] Frommenwiler, D. A., Reich, E., Sharaf, M. H. M., Canigueral, S., & Etheridge, C. J. (2022). Investigation of marker herbal products regulated under different categories. How can HPTLC help to detect quality problems? *Frontiers in Pharmacology*. 13.
[212] Booker, A., Agapouda, A., Frommenwiler, D. A., Scotti, F., Reich, E., & Heinrich, M. (2018). St John's wort (*Hypericum perforatum*) products – an assessment of their authenticity and quality. *Phytomedicine. 40*, 158-164.
[213] Brusač, E., Jeličić, M. L., Nigović, B., Amidžić Klarić, D., & Mornar, A. (2022). Determination of curcuminoids, piperine, boswellic acids and andrographolides in food and dietary supplements by HPLC. *Food Technology and Biotechnology*. *60*, 434-448.
[214] Gafner, S., Blumenthal, M., Foster, S., Cardellina, J. H., Khan, I. A., & Upton R. (2023). Botanical ingredient forensics: detection of attempts to deceive commonly used analytical methods for authenticating herbal dietary and food ingredients and supplements. *Journal of Natural Products*. *86*, 460-472.
[215] Liang, Z., Hu, H., Li, J., Yao, D., Wang, Y., & Ung, C. O. L. (2021). Advancing the regulation of traditional and complementary medicine products: A comparison of five regulatory systems on traditional medicines with a long history of use. *Evidence-Based Complementary and Alternative Medicine.* 5833945.
[216] Lovelace, Jr., B. (2023, August 11). How a critical cancer drug became hard to find in the U.S. *NBC News*. Retrieved April 13, 2025 from https://www.nbcnews.com/specials/cisplatin-shortage-cancer-drug-chemotherapy-us/index.html.
[217] Uhl, A., Schmidt, A., Jensch, C., Köster, D., & Strube, J. Development of concepts for a climate-neutral chemical-pharmaceutical industry in 2045. *Processes. 10*, 1289.
[218] Wu, J., Li, X., Huang, L., Meng, X., Hu, H., Luo, L., & Chen, S. (2019). A new GIS model for ecologically suitable distributions of medicinal plants. *Chinese Medicine. 14*, 4.
[219] Wang, H., Zhang, C., Zhao, L., Xing, X., & Cao, Y. (2025). Analysis of geographic suitability of Chinese medicine based on analytic hierarchy process-fuzzy. *Sensors and Materials*. *37*, 261-268.
[220] Bom, S., Jorge, J., Ribeiro, H. M., & Marto, J. (2019). A step forward on sustainability in the cosmetics industry: A review. *Journal of Cleaner Production. 225*, 270-290.
[221] Daley, S.-k., & Cordell, G. A. (2021). Sustainable phytocosmetics. In *Phytocosmetics and Cosmetic Science*. (Eds.) Lourith, N., & Tsim, K. Boca Raton, FL: Taylor & Francis, CRC Press.
[222] Rocca, R., Acerbi, F., Fumagalli, L., & Taisch, M. (2022). Sustainability paradigm in the cosmetics industry: State of the art. *Cleaner Waste Systems. 3*, 100057.
[223] Martins, A. M., & Marto, J. M. (2023). A sustainable life cycle for cosmetics: From design and development to post-use phase. *Sustainable Chemistry and Pharmacy. 35*, 101178.
[224] Frix, A. (2022). F & F ingredients: A changing market. *IFEAT World. 10* (July), 18-26.
[225] Elterlein, F., Bugdahn, N., & Kraft, N. (2024). Sniffing out the sustainable future: The renewability revolution in fragrance chemistry. *Chemistry – European Journal. 30*, e202400006.
[226] Rinsema, T. J. (1999). One hundred years of aspirin. *Medical History. 43*, 502-507.
[227] Wainwright, M., & Kristiansen, J. E. (2011). On the 75th anniversary of Prontosil. *Dyes and Pigments*. *88*, 231-234.
[228] Guner, O. F. (2002). History and evolution of the pharmacophore concept in computer-aided drug design. *Current Topics in Medicinal Chemistry. 2*, 1321-1332.
[229] Lombardino, J. G., & Lowe, III, J. A. (2004). The role of the medicinal chemist in drug discovery - then and now. *Nature Reviews Drug Discovery. 3*, 853-862.
[230] Vandanyan, R., & Hraby, V. (2006). *Synthesis of Essential Drugs*. The Netherlands, Amsterdam: Elsevier Publisher. pp. 617.

[231] Liu, D., Fu, J.-M, Xiao, X.-M., Chen, D.-Y. Geng, A.-S., Sun, Y.-G., & Wang, Y. (2005). Origin and appraisal of coal derived gas and oil. *Petroleum Exploration and Development*. *32*. 137-141.
[232] Xu, C., Nasrollahzadeh, M., Selva, M., Issaabadi, Z., & Luque, R. (2019). Waste to wealth: biowaste valorization into valuable bio(nano)materials. *Chemical Society Reviews. 48*, 4791-4822.
[233] Kircher. M. (2025). Chemical production based on biomass - potential and limits. *Biomass 5*, 8.
[234] Smanski, M. J., Peterson, R. M., Rajski, S. R., & Shen, B. (2009). Engineered *Streptomyces platensis* strains that overproduce antibiotics platensimycin and platencin. *Antimicrobial Agents and Chemotherapy*. *53*, 1299-1304. https://doi.org/10.1128/aac.01358-08.
[235] Zhang, M.-Q., Gaisser, S., Nur-e-Alam, M., Sheehan, L. S., Vousden, W. A., Gaitatzis, N., Peck, G., Coates, N. J., Moss, S. J., Radzom, M., Foster, T. A., Sheridan, R. M., Gregory, M. A., Roe, S. M., Prodromou, S. C., Pearl, L., Boyd, S. M., Wilkinson, B., & Martin, C. J. (2008). Optimizing natural products by biosynthetic engineering: discovery of nonquinone Hsp90 inhibitors. *Journal of Medicinal Chemistry*. *51*, 5494-5497.
[236] Carter, G. T. (2011). Natural products and pharma 2011. Strategic changes spur new opportunities. *Natural Product Reports*. *28*, 1783-1789.
[237] Pereira, R. (2009). The seven wastes. *Isixsigma Magazine. 5*, 1-3.
[238] Environmental Protection Agency. National Overview: Facts and Figures on Materials, Wastes and Recycling. Retrieved April 13, 2025 from https://www.epa.gov/facts-and-figures-about-materials-waste-and-recycling/national-overview-facts-and-figures-materials.
[239] McHugh, T. H. (2025). Food loss and waste: A multi-billion-dollar opportunity. Retrieved April 13, 2025 from https://www.usda.gov/sites/default/files/documents/Combined.pdf.
[240] Orsato, R. J., & Wells, P. (2007). The automobile industry & sustainability. *Journal of Cleaner Production. 15*, 989-993.
[241] Anderberg. S. (1998). Industrial metabolism and linkages between economics, ethics, and the environment. *Ecological Economics*. *24*, 311-320.
[242] Beddall, B. G. (1968). Wallace, Darwin, and the theory of natural selection. *Journal of the History of Biology. 1*, 261-323.
[243] Geissdoerfer, M., Savaget, P., Bocken, N. M. P., & Hultink, E. J. (2017). The circular economy – a new sustainability paradigm. *Journal of Cleaner Production*. *143*, 757-768.
[244] European Commission. (2020, March 11). *Circular Economy Action Plan*. EUR-Lex. 52020DC0098. Retrieved March 31, 2025 from https://eur-lex.europa.eu/legal-content/EN/TXT/?qid=1583933814386&uri=COM:2020:98:FIN. \
[245] Lizundia, E., Luzi, F., & Puglia, D. (2022). Organic waste valorisation towards circular and sustainable biocomposites. *Green Chemistry. 24*, 5429-5459.
[246] Mishra, K., Siwal, S. S., Nayaka, S. C., Guan, Z., & Thakur, V. K. (2023). Waste-to-chemicals: Green solutions for bioeconomy markets. *Science of the Total Environment. 887*, 164006.
[247] Venkateswarlu, K. (2021). Ashes from organic waste as reagents in synthetic chemistry: A review. *Environmental Chemistry Letters. 19*, 3887-3950.
[248] Afanasenko, A., & Barta, K. (2021). Pharmaceutically relevant (hetero) cyclic compounds and natural products from lignin-derived monomers: present and perspectives. *iScience, 24*, 102211.
[249] Afanasenko, A. M., Wu, X., De Santi, A., Elgaher, W. A. M., Kany, A. M., Shafiei, R., Schulze, M.-S., Schulz, T. F., Haupenthal, J., Hirsch, A. K. H., & Barta, K. (2024). Clean synthetic strategies to biologically active molecules from lignin: a green path to drug discovery. *Angewandte Chemie, International Edition. 63*, e202308131.
[250] Jadhav, P., Bhuyar, P., Misnon, I. I., Rahim, M. H. Ab., & Roslan, R. (2024). Advancement of lignin into bioactive compounds through selective organic synthesis methods. *International. Journal of Biological Macromolecules. 276 Pt.2*, 134061.
[251] Orooji, Y., Han, N., Nezafat, Z., Shafiei, N., Shen, Z., Nasrollahzadeh, M., Karimi-Maleh, H., Luque, R., Bokhari, A., & Klemeš, J. J. (2022). Valorisation of nuts biowaste: Prospects in sustainable bio(nano)catalysts and environmental applications. *Journal of Cleaner Production. 347*, 131220.
[252] Rachwał, K., Waśko, A., Gustaw, K., Polak-Berecka, M. (2020). Utilization of brewery wastes in food industry. *PeerJ. 8*, e9427.
[253] Sarangi, P. K., Singh, T. A., Singh, N. J., Shadangi, K. P., Srivastava, R. K., Singh, A. K., Chandel, A. K., Pareek, N., & Vivekanand V. (2022). Sustainable utilization of pineapple wastes for production of bioenergy, biochemicals and value-added products: a review. *Bioresource Technology*. *351*, 127085.

[254] Sneddon, H. (2014). Embedding sustainable practices into pharmaceutical R&D: what are the challenges? *Future Medicinal Chemistry*. *6*, 1373-1376.
[255] Bryan, M. C., Dunn, P. J., Entwistle, D., Gallou, F., Koenig, S. G., Hayler, J. D., Hickey, M. R., Hughes, S., Kopach, M. E., Moine, G., Richardson, P., Roschangar, F., Steven, A., & Weiberth, F. J. (2018). Key green chemistry research areas from a pharmaceutical manufacturers' perspective revisited. *Green Chemistry*. *20*, 5082-5103.
[256] Mycroft, M., Gomis, M., Mines, P., Law, P., & Bugg, T. D. H. (2015). Biocatalytic conversion of lignin to aromatic dicarboxylic acids in *Rhodococcus jostii* RHA1 by re-routing aromatic degradation pathways. *Green Chemistry*. *17*, 4974-4979.
[257] Chen, X., Song, S., Li, H., Gözaydln, G., & Yan, N. (2021). Expanding the boundary of biorefinery: organonitrogen chemicals from biomass. *Accounts of Chemical Research*. *54*, 1711-1722.
[258] Karlen, S. D., Timokhin, V. I., Sener, C., Mobley, J. K., Runge, T., & Ralph, J. (2024). Production of biomass-derived *p*-hydroxybenzamide: Synthesis of *p*-aminophenol and paracetamol. *ChemSusChem 17*, e202400234.
[259] Qiang, G., Ansari, Mohd. F., Sun, Z., & Elangovan, S. (2024). Bioactive molecules from lignocellulose-derived platform chemicals. *Advanced Synthesis and Catalysis. 366*, 4805-4834.
[260] Deuss, P. J., Scott, M., Tran, F., Westwood, N. J., De Vries, J. G., & Bartam K. (2015). Aromatic monomers by *in situ* conversion of reactive intermediates in the acid-catalyzed depolymerization of lignin. *Journal of the American Chemical. Society. 137*, 7456-7467.
[261] De Santi, A., Galkin, M. V., Lahive, C. W., Deuss, P. J., & Barta, K. (2020). Lignin-first fractionation of softwood lignocellulose using a mild dimethyl carbonate and ethylene glycol organosolv process. *ChemSusChem 13*, 4468-4477.
[262] Cho, E. J., Trinh, L. T. P., Song, Y., Lee, Y. G., & Bae, H. J. (2020). Bioconversion of biomass waste into high value chemicals. *Bioresource Technology*, *298*, 122386.
[263] Coscieme, L., Mortensen, L. F., Anderson, S., Ward, J., Donohue, I., & Sutton, P. C. (2020). Going beyond Gross Domestic Product as an indicator to bring coherence to the Sustainable Development Goals. *Journal of Cleaner Production. 248*, 119232.
[264] Costanza, R. (2023). To build a better world, stop chasing economic growth. *Nature. 624*, 519-521.
[265] van den Bergh, J. C. J. M. (2009). The GDP paradox. *Journal of Economic Psychology. 30*, 117-135.
[266] Giannetti, G.B., Agostinho, F., Almeida, C. M. V. B., & Huisingh, D. (2015). A review of limitations of GDP and alternative indices to monitor human wellbeing and to manage eco-system functionality. *Journal of Cleaner Production. 87*, 11-25.
[267] Mill, J. S. (1909). *Principles of Political Economy with Some of their Applications to Social Philosophy 7th ed.* Ashley, Sir W. J. (Ed.). London, UK: Longmans, Green and Co.
[268] Rockström, J., Steffen, W., Noone, K., Persson, Å., Chapin III, F. S., Lambin, E., Lenton, T.M., Scheffer, M., Folke, C., Schellnhuber, H. J., Nykvist, B., de Wit, C. A., Highes, T., van der Leeuw, S., Rodhe, H., Sörlin, S., Snyder, P. K., Costanza, R., Svedin, U., (….), & Foley, J. (2009). Planetary boundaries: exploring the safe operating space for humanity. *Ecology and Society. 14*, no. 2, pp. 33.
[269] Steffen, W., Richardson, K., Rockström, J., Cornell, S. E., Fetzer, I., Bennett, E. M., Biggs, R., Carpenter, S. R., de Vries, W., de Wit, C. A., Folke, C., Gerten, D., Heinke, J., Mace, G. M., Persson, L. M., Ramanathan, V., Reyers, B., & Sörlin, S. (2015). Planetary boundaries: Guiding human development on a changing planet. *Science. 347*, 1259855.
[270] Richardson, K., Steffen, W., Lucht, W., Bendtsen, J., Cornell, S. E., Donges, J. F., Drüke, M., Fetzer, I., Bala, G., von Bloh, W., Feulner, G., Fiedler, S., Gerten, D., Gleeson, T., Hofmann, M., Huiskamp, W., Kummu, M., Mohan, C., Mogués-Bravo, D., (….), & Rockström, J. (2023). Earth beyond six of nine planetary boundaries. *Science Advances. 9*, eadh2458.
[271] Haberl, H., Wiedenhofer, D., Virág, D., Kalt, G., Plank, B., Brockway, P., Fishman, T., Hausknost, D., Krausmann, F., Leon-Gruchalski, B., Mayer, A., Pichler, M., Schaffartzik, A., Sousa, T., Streek, J., & Creutzig, F. (2020). A systematic review of the evidence on decoupling of GDP, resource use and GHG emissions, Part II: Synthesizing the insights. *Environmental Research Letters. 15*, 065003.
[272] Vadén, T., Lähde, V., Majava, A., Järvensivu, P., Toivanen, T., Hakala, E., & Eronen, J. T. (2020). Decoupling for ecological sustainability: A categorisation and review of research literature. *Environmental Science & Policy. 112*, 236-244.

MALAYSIAN NATURAL PRODUCTS SOCIETY

[273] Ripple, W. J., Wolf, C., Newsome, T.M., Galetti, M., Alamgir, M., Crist, E., Mahmoud, M. I., Laurance, W.F., & 15,364 scientist signatories from 184 countries. (2017). World scientists' warning to humanity: a second notice. *BioScience. 67*, 1026-1028.
[274] Monbiot, G. (2021, September 29). "Green growth" doesn't exist – less of everything is the only way to avert catastrophe. *The Guardian*. Retrieved May 6, 2025. From https://www.theguardian.com/commentisfree/2021/sep/29/green-growth-economic-activity-environment.
[275] Puschmann, T., & Alt, R. (2016). Sharing economy. *Business and Information Systems Engineering. 58*, 93-99.
[276] Dellaert, B. G. C. (2019). The consumer production journey: marketing to consumers as co-producers in the sharing economy. *Journal of the Academy of Marketing Science. 47*, 238-254.
[277] Daly, H. E. (1996). *Beyond Growth. The Economics of Sustainable Development*. Boston, MA; Beacon Press.
[278] Cook, E. (1982). The consumer as creator: a criticism of faith in limitless ingenuity. *Energy Exploration and Exploitation. 1*, 189-201.
[279] Latouche, S. (2009). *Farewell to Growth*. Cambridge, UK: Polity Press. pp. 180.
[280] Kallis, G., Kerschner, C., & Martinez-Alier, J. (2012). The economics of degrowth. *Ecological Economics. 84*, 172-180.
[281] Hickel, J. (2021). What does degrowth mean? A few points of clarification. *Globalizations. 18*, 1105-1111.
[282] Mathevet, R., Bousquet, F., & Raymond, C. M. (2018). The concept of stewardship in sustainability science and conservation biology. *Biological Conservation. **217***, 363-370.
[283] Bourdeau, Ph. (2004). The man-nature relationship and environmental ethics. *Journal of Environmental Radioactivity. 72*, 9-15.