Materials of biological origin and biofuels: Small environmental footprint and epigenetic impact (Review)

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Abstract. Human activity, specifically the overreliance on fossil resources, has had numerous adverse effects on the environment and an epigenetic impact on human health. The destabilization of the environment and the accumulation of waste have caused alterations in the stability of the human ecosystem, affecting the exposome and modifying the epigenetic mechanisms that control or deregulate human physiology. For example, the increasing use of plastics and the chemicals derived, have been shown to promote diseases by altering epigenetic patterns. Thus, there is a growing need for more environmentally- and human-friendly alternatives, also known as 'green products and fuels'. Environmental biotechnology aims to produce 'green' products and fuels through the use of living cells and cell-derived molecules. The solutions offered by this scientific discipline may include 'green' alternatives to chemical solvents, machine lubricants, plastics, machine fuel and batteries. Each of these alternatives has its own strengths and weaknesses that should be taken into consideration before being heralded as the successors of fossil-derived products. The present review article summarizes the current scientific knowledge on the epigenetic impact of the current environmental status and the benefit of these alternatives.

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Contents

1. Introduction

The natural environment contains the Earth's living organisms, air, soil and water (1). Alterations in the natural environment may have profound effects on social and economic development, human health and lifestyle, as well as on biological processes through an epigenetic impact (2). Therefore, it is crucial to study alterations in the natural environment and develop approaches with which to mitigate or even reverse possible adverse effects produced. Human activities, such as urbanization and pollution have led to the occurrence of a number of changes in the natural environment (3). In particular, anthropogenic activities have caused severe alterations in the Earth's climate (4). The effects of climate change include extreme weather and climatic events, water and food scarcity, ocean acidification and rising sea levels, damage to ecosystems and biodiversity, the disruption of the social infrastructure, and may damage human health (5).

The environmental footprint is a metric used to study the association between humans and their natural environment, and to examine the effect a population's consumption or lifestyle has on the environment (6). Environmental footprints consider several parameters regarding the environment, such as climate change, ocean acidification and rising sea levels, water scarcity and pollution, land availability, chemical pollution and loss of biodiversity (7). By studying the environmental footprints of various human activities and product use, specific approaches can be developed to mitigate their negative effects on the environment. Several factors that have a negative effect on the environmental footprint may also have an immediate negative effect on human health. This effect is mainly achieved through epigenetic mechanisms. Epigenetics refers to information that exists beyond that encoded in the DNA sequence and helps transduce the inheritance of gene expression patterns without DNA sequence alteration (8). Several mechanisms underlie epigenetics, such as DNA methylation, histone modifications and interaction with non-coding RNA molecules (9). The effect that such factors may have on epigenetics is one of the main subject of a study field termed environmental epigenetics (10).

The majority of countries rely on fossil fuels, which consist of oil, coal and natural gas for their energy needs (11). Fossil fuel combustion by-products are some of the most significant contributors to climate change (12). In the early 2010s, >80% of human energy was derived from fossil fuels (13). Emissions from fossil fuels include carbon dioxide (CO_2), which plays an important role in the greenhouse effect (12). The greenhouse effect is a system that drives Earth's surface heating. Solar radiation passes mostly effortlessly through the atmosphere and heats the Earth's surface. Consecutively, energy is reemitted as infrared, a large part of which is absorbed by CO_2 and water vapor in the atmosphere, thus acting as a blanket surrounding Earth. Under normal circumstances, the greenhouse effect maintains the planet's average surface temperature viable to humans. Excess CO_2 produced by fossil fuels, though, enhances the natural greenhouse effect and warms the planet at an alarming rate (14). Moreover, fossil fuel extraction, transportation, distribution and waste management also have adverse effects on the environment (13). The necessity for sustainable energy, i.e., able to supply a growing global population needs without destroying the environment within which it is used, has become more than necessary (15). Additionally, fossil fuel burning produces large amounts of polycyclic aromatic hydrocarbons (PAHs). Early embryo exposure to PAHs results in alterations in DNA methylation levels, with a prime example being the hypermethylation of the acyl-CoA synthetase long chain family member 3 (ACSL3) gene promoter, which leads to the decreased expression of the mentioned gene. The aforementioned condition is associated with asthma symptoms in children (10).

Another human activity with a damaging environmental footprint is the extensive use of plastics (16). Although inexpensive, lightweight and durable, plastics pose a credible environmental threat (16). Some of the negative effects of the extensive use of plastics include waste accumulation in landfills and natural habitats, physical issues in wildlife due to ingestion or entanglement in plastic, chemicals seeping from plastic products and their subsequent transfer to wildlife and humans (17). Additionally, plastics used in various medical procedures may feature various pathogens, and their management and destruction have a severe environmental footprint (18).

The negative effects of the use of plastics do not only apply to the macroscopic level of the environmental footprint, but have also been implicated in a number of human pathogenies through an epigenetic effect. Chemicals used for manufacturing plastics, such as bisphenols and phthalates (plastics derived endocrine disruptors) have been shown to induce toxic epigenetic effects in both male and female fertility, affecting their reproductive ability and quality of gametes (19). Prenatal exposure to bisphenols and phthalates has been proven to promote epigenetic modifications in embryo development, resulting in offspring pathophysiology, with a significant association with an increased incidence of diseases, such as obesity, reproductive diseases and impaired brain development (20,21). The recent study by Engdahl *et al* (22) negatively associated cognitive functions with prenatal bisphenol F exposure, demonstrating lower IQ levels in 7-year-old children. Bisphenol-A (BPA), an estrogen mimic, is a widely studied plastic-derived chemical, that modifies epigenetic signs, and affects DNA methylation patterns and histone modifications, induces transcriptional modifications, regulates gene expression and affects miRNA expression (23). The BPA epigenetic risk has been linked to metabolic disorders, hepatic deficiencies, type II diabetes, cardiovascular diseases and hypertension risk, as well as to hormone-dependent cancers, such as breast and prostate cancer (24-28). BPA is also characterized as a potential risk factor for neurodevelopmental disorders, such as autism (29). Plastic-derived chemicals are major risk factors that are epigenetically involved in fetal, natal and offspring development, and in the progression of diseases, and in some cases have been shown to promote transgenerational inheritance (20). It is thus imperative to lessen plastic use and develop new materials with a smaller environmental footprint and minimize the adverse effects of their epigenetic impact.

Biotechnology is a multidisciplinary study field that makes use of varied tools and technologies to create products based on cells or cell-derived molecules (30). Environmental biotechnology, which studies topics, such as waste management, biodegradation and biofuel production, aims to mitigate a number of deleterious anthropogenic environmental alterations (31). Furthermore, incorporating information extracted from environmental epigenetics can help design products that also have no deleterious effect on human health. The present review article presents biotechnological alternatives that lessen some of the environmental concerns and epigenetic effects associated with the aforementioned products.

2. Materials of biological origin

The main goal in multiple scientific disciplines is to incorporate the functional properties of materials of biological origin into new materials. Materials of biological origin are of significant interest when it comes to designing environmentally friendly, also known as 'green' products. Biological feedstocks, specifically, can be used to produce solvent, plastic and lubricating oil alternatives (32).

Solvents are extensively used in the production of chemicals as media for chemical reactions and chemicals separation or purification (33). The majority of solvents are highly volatile, flammable, toxic and can cause severe air pollution (34). These solvent attributes cause a number of environmental concerns, which mainly focus on solvent synthesis, use and disposal (33). Furthermore, some industrial solvents, such as trichloroethylene (TCE) have been shown to be associated with various autoimmune diseases, including lupus and scleroderma. This association may be due to the fact that TCE exposure leads to differentially methylated CpGs in regions responsible for polycomb group proteins binding. These proteins' function is to regulate T effector cell expansion and differentiation (35). Biobased solvents are a possible solution to the environmental and health concerns presented by traditional chemical solvents. Biobased solvents are generally derived from agricultural crops rich in carbohydrates, such as corn, wheat, beets, or residual organic matter, and are generally less toxic and volatile than traditional chemical solvents (36). These characteristics of biobased solvents render them a 'greener' option than traditional chemical solvents. Alcohols produced through the fermentation of biomass include 1-butanol, oc-tan-2-ol and propane-1,3-diol, and can be used as solvents in numerous industrial processes and may aid the production of commercial antibiotics, vitamins, resins, paint coatings and adhesives (36). Another prime example of a biobased solvent is ethyl lactate, which is biodegradable and non-toxic, and showcases a low volatility. Ethyl lactate garnered by corn and soybeans through the fermentation of biomass and the reaction of two fermentation products, ethanol and lactic acid. Ethyl lactate is mainly used in the extraction of phytochemicals (37). Although extremely promising, it should be noted that not all biobased solvents are of no environmental consequence. For example, terpenes are toxic to fish, while obtaining acetic acid from corn carbohydrate leads to higher emissions of greenhouse gasses than the production of its' fossil fuel-based counterpart (37).

Lubricating oils are essential in machine and device operation, since they minimize friction, eliminate the scuffing of rubbing machine elements, help with machine cooling, have anti-corrosion properties, and wash away carbon deposits and microparticles (38). Lubricating oils are a mixture of base oils that are derived from crude oils and enriching additives, which are mostly products of an organic synthesis process (38). Crude oil is a fossil resource that consists of paraffinnic, cycloparaffinic and aromatic hydrocarbons, low percentages of sulfur, and traces of nitrogen and oxygen compounds (39). Crude oil exerts severe toxic effects on the environment (40). Additives provide lubricating oils with new useful properties, enhance their existing properties and improve product lifetime (41). Traditional additives include sulfonate, sulfide alkylphenols and dialkyl dithiophosphate, which cause detrimental environmental effects (42). Lubricants were also used to contain polychlorinated biphenyls (PCBs) up until the 1970s when they were banned; they functioned as endocrine disruptors which altered gene methylation and were shown to exert carcinogenic effects (43). The effect of PCBs on the environment and human health have instilled a cautionary approach in the production of lubricants or novel additives. The aforementioned information indicates that there is a need for 'greener' and healthier alternatives to both lubricating oils and their additives. Non-fossil-based natural oils are an enticing option when it comes to lubricants with a small environmental footprint. These so-called biolubricants include natural vegetable oils, such as rice bran oil, rapeseed oil and coconut oil. Biolubricants have exhibited potential as they are characterized by a high bioavailability, high biodegradability, the absence of toxic and polluting effects to the environment, and, with the right additives, identical lubrication properties to those of petrochemical lubricants (44). Moreover, nanomaterials can be used as environmentally friendly additives. A prime example are nano-additives based on reduced graphene oxide nanosheets, which display a cost-effective and relatively straightforward, environmentally friendly synthesis process (45).

The environmental and epigenetic impact of plastics has already been mentioned. Plastics are synthetic polymers consisting of small molecules, termed monomers, linked together in a repetitive manner (46). The vast majority of plastics are non-biodegradable and the monomers used to construct them are derived from fossil hydrocarbons (47). The aforementioned, in conjunction with the fact that synthetic polymers are produced on an enormous scale annually, renders the management of plastics and the development of 'greener' alternatives a main goal of environmental biotechnology (48). Additionally, and as already mentioned, since the majority of plastics release chemicals with estrogenic activity, their use may lead to the disruption of the function of the endocrine system of an organism, culminating in severe pathological conditions (49). Some of these endocrine disruptors have been shown to influence both the methylation of regions, including hormone response elements and mediators of histone modifications (50). Bioplastics appear to be an appealing alternative to traditional plastics. The term bioplastics refers to biodegradable plastic materials and/or plastics that are produced from renewable resources (51). It is also important to note that, although some bioplastics are produced from renewable natural resources, not all are biodegradable (52). Bioplastics based on fossil materials are designed by selecting the appropriate monomers, additives and the polymerization process in order to become biodegradable products (53). Such types of plastics include polycaprolactone (PCL), poly-butylene succinate (PBS) and polybutylene adipate (PBA) (52). Bioplastics based on renewable natural resources (biobased plastics) are produced through fermentation or chemical processes, or a mixture of biotechnological and chemical processes (54). Biodegradable biobased plastics include polylactic acid (PLA), polyhydroxyalkanoates (PHAs), succinic acid, 1,3-propanediol-based polymers, cellulose and starch (52,54). Non-biodegradable biobased plastics are chemically identical to their fossil-based counterparts, and thus also exhibit identical chemical properties. These non-biodegradable biobased plastics are also known as 'drop-in plastics' due to their low need for major investment and include biobased polyethylene terephthalate (bio-PET) and biobased polyethylene (bio-PE). The selection of an appropriate bioplastic depends on several parameters, such as a the lifetime of a product and resistance to environmental influences (53). In the cases of plastics used for product packaging, biodegradable biobased plastics seem to be an enticing option with a small environmental footprint (55).

Apart from providing alternatives to traditional synthetic plastics, environmental biotechnology aims to address the issue of already existing plastic waste. The current methods of managing plastic waste are landfill depositing, recycling and incineration (56). These methods have severe drawbacks however. Specifically, plastics in landfills last for an extensive period of time and render the ground unfit for profitable use; plastic recycling is very costly, and incineration releases toxic gases into the environment (56). A proposed solution is the use of microorganisms and enzymes to degrade synthetic plastics. Several enzymes and microorganisms that act on synthetic polymers have plastic-degrading abilities (57). However, a current bottleneck exists in the initial degradation of robust polymers with a high molecular weight (48). Therefore, further research is required for the identification of novel depolymerases that render the initial breakdown of plastics more efficient (57). Nonetheless, current advances in synthetic biology may overcome such a hurdle by generating synthetic microorganisms with the desired plastic-degrading abilities (48).

3. Biofuels

As it has already been mentioned, fossil fuel extraction is relatively harmful to the environment and its combustion products have a severe impact on human health. Biofuels may be a 'green' alternative to traditional fossil fuel, with biofuel research markedly increasing over the past decades. Biofuel refers to fuel obtained by biomass through a chemical procedure as opposed to a slow geological process, such as common fossil fuel (58). Biofuels include bioethanol, biomethane, biodiesel and biobutanol (59). The production of biofuels involves organic biomass, which is thermally and chemically decomposed or fermented by microorganisms to produce liquid or gas fuels, such as ethanol, methane and hydrogen (59). The theoretical benefits of biofuels include a reduction in oil import dependency, a more secure energy supply, an increased socioeconomic support of rural areas, and a smaller environmental footprint (60). As regards the health-related effects of biofuel use, further research is warranted. A comparative study on biodiesel produced by waste cooking oil and conventional fossil diesel as diesel engine fuel demonstrated that the fractions of parent PAHs gradually decreased with the increasing biodiesel content in the blends, while the corresponding fractions of oxygenated and nitrated derivatives steadily increased, particularly for oxy-derivate PAHs (61). Biofuels are divided into different generations, depending on their origin and production method (Fig. 1) (62).

First-generation (1G) biofuels are produced primarily from food crops, such as grains, sugar canes and vegetable oils (63). 1G bioethanol, specifically, is, as of 2019, the main liquid biofuel produced worldwide (64). Although 1G biofuels appear to be a step towards energy production with a lower environmental footprint, their use garnered much controversy in the 21st century, since the use of food crops and oils to produce fuel had a negative impact on food quality and undermined food safety. Landowners may begin to disproportionally use their edible crops for fuel rather than for food production, which, in turn, may lead to a decreased food supply and subsequent increases in prices (63). Moreover, some 1G biofuel production pathways seem to offer no advantage when it comes to lowering greenhouse gas emissions due to nitrous oxide (N_2O) emissions, peat oxidation in the case of cultivation on peatland soils and the use of fertilizers (65). Lastly, the high demand for 1G biofuels may lead to problematic changes in land use (64). The aforementioned information indicates that the sustainability of 1G biofuels is severely limited, although ethanol produced by sugar canes is a possible exception, since it meets biofuel sustainability criteria (66). It is important to mention though, that the production of 1G biofuels, such as sugarcane ethanol will continue to improve and may thus may continue to satisfy energy needs (66).

The aforementioned disadvantages of several 1G biofuels led to the development of more sustainable biofuels, which subsequently led to the development of second-generation (2G) biofuels. 2G biofuels use non-food lignocellulosic materials, such as dedicated energy crops including perennial grasses and short rotation forestry, woodchips from energy crops, agricultural and forest residues, and even low-valued municipal and industrial solid wastes as raw materials (67). 2G biofuels overcome the dilemma 'food vs. fuel' dilemma since they do not use edible crops, and thus do not negatively impact food production and quality. Additionally, certain 2G biofuels such as cellulosic ethanol from switchgrass and carbon-negative biofuels from low-input high-diversity grassland biomass require a lower agricultural input, i.e., less fertilizer, pesticide and energy (68). The main disadvantage of 2G biofuels is their production cost. 2G biofuels have a higher capital cost than 1G biofuels. At the same time, some estimations in the early 2010s demonstrated that 2G biofuels may be two- to three-fold more expensive than petroleum fuels on an energy equivalent basis (69,70). Moreover, several mechanical hurdles have prevented 2G biofuels from reaching their optimal productivity (60). Specifically, 2G biofuels face technical difficulties during pre-treatment processes, and the conversion of lignocellulosic materials is quite inefficient due to the complex structure of the materials (71). Thus, further research is required in order for 2G biofuels to reach their potential and become commercially enticing.

Third-generation (3G) biofuels aim to address the disadvantages of 2G biofuels by using algae-derived biomass as their energy source (71). Algae comprise a diverse group of species that include photosynthetic, oxygen-producing, unicellular, or multicellular organisms without embryophyte terrestrial plants and lichens (72). Algae biomass consists of biochemical molecules, such as carbohydrates, lipids and proteins (73). Algae biomass presents numerous advantages as a source of biofuel, such as the ability to grow throughout the year, the ability to grow under variable conditions and a high growth potential (74). Furthermore, processing algae biomass can provide a number of economically enticing co-products, such as ingredients for functional foods and cosmetics (75). Even so, biofuel produced from currently available algae species does not seem to be cost-competitive with traditional fossil fuels and thus, selective breeding and genetic engineering are required to provide economically viable strains (76).

Fourth-generation (4G) biofuels are based on raw materials that are the result of genetic engineering, metabolic engineering, and synthetic biology applications on algae and cyanobacteria (77). These biofuels have a number of advantages in comparison to 3G biofuels. 4G biofuels use biomass with an enhanced carbohydrate and lipid content for optimal energy production (78). Additionally, genetically engineered algae can exhibit an enhanced CO_2 sequestration (79). Despite these promising abilities, though, 4G biofuels are in their early stage of development, and thus the investments needed to expand further the technology are relatively high.

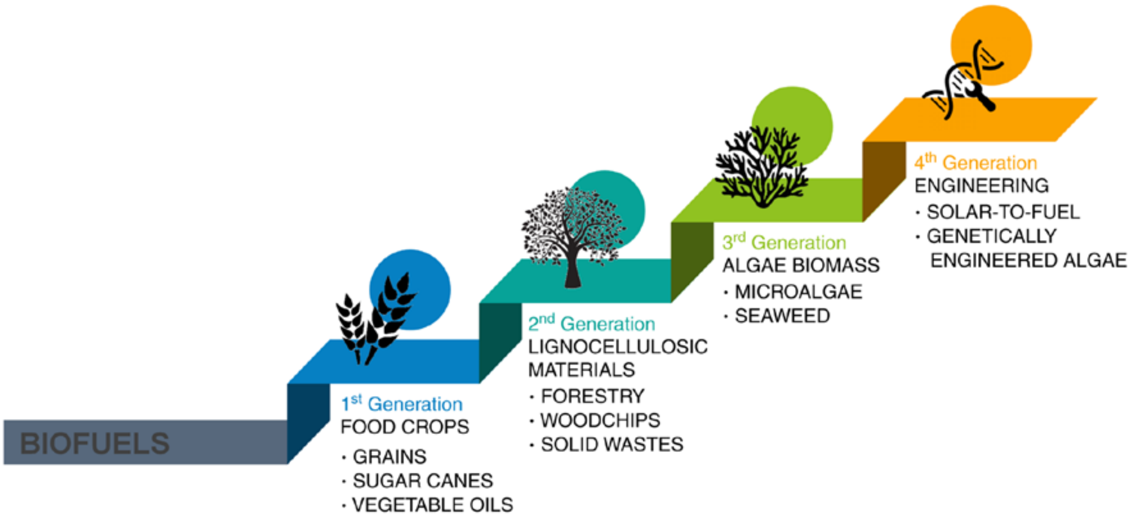

Figure 1. Biofuels and their different generations depending on their origin and production method.

4. Biobatteries

When it comes to environmental biotechnology and the introduction of 'greener' energy, a brief mention should also be made of biobatteries, such as microbial fuel cells (MFCs). After being disposed of, traditional batteries, such as one-use AA alkaline batteries used in numerous household appliances and rechargeable lithium batteries used in modern consumer electronic products can be considered as hazardous waste. This fact is mainly due to the potential leaching of toxic materials to the ecosystem (80,81). Moreover, nickel, a metal used for the production of batteries has been implicated in multiple respiratory system conditions, from mild irritations to cancer. Nickel has been shown to alter DNA methylation with a prime example being the hypermethylation of the *O*-6-methylguanine-DNA methyltransferase (MGMT) promoter, a condition associated with lung cancer. Furthermore, nickel exposure has been shown to affect the general levels of histone modifications, implying a severe and global gene expression deregulation (82). Biobatteries or biological fuel cells are electro-biochemical devices that convert organic compounds, such as glucose and starch to electricity through the use of low-cost bio-catalyst enzymes and microorganisms (83). Such batteries are highly safe and biodegradable alternatives to traditional batteries. Research on biobatteries, though, is in its early stages and some technical issues, such as long-term stability need to be overcome (84).

5. Current applications of 'green' products

The majority of these 'green' products have been shown to have several market applications. Biodiesel may be the optimal example of a 'green' product that already competes with traditional products on the market level. Biodiesel blends, which include a mixture of pure biodiesel and petrodiesel are useable in any diesel engine, with pure biodiesel being usable through the installation of a heating system. Biodiesel is currently produced at the million gallons level annually by industrial facilities and by small manufacturers that produce it from used cooking oil (85). Biolubricants, which address the environmental and health concerns of traditional lubricants, have also exhibited an increase in consumption with a prime example being that 4% of 1.05 million tons of the total lubricants in 2005 in Germany were biolubricant, with their use increasing rapidly (86). Recent technological advancements have also demonstrated that biobatteries, such as bacteria-powered ones, can be an excellent energy source for low-power battery-reliant devices, since they are stand-alone device platforms that can be used in resource-limited and remote regions (87). Bioplastics have also displayed several market applications with the most common ones being packaging material, and carrier and compost bags. It should also be mentioned that biodegradable polymers have been a mainstay of biomedicine (88). Lastly, biobased solvents also seem to display an increase in use. Specifically, the global annual global solvent market is ~20 million metric tons, with biobased solvents being estimated to amount to one million metric tons in Europe (89).

6. Conclusions and future perspectives

The environmental footprint has been a major concern over the past decades in terms of the global economy, environmental health and human health. Fossil resources that have served human needs for a long period of time have been responsible for the detrimental effects on the planet. The destabilization of the environment and the accumulation of waste have multiple negative impacts on humans, not only as direct health issues, but also in an epigenetic perspective. The resources used for energy production, and high-waste energy and resources consumption have caused alterations in the stability of the human ecosystem, altering the chemical composition of the environment and affecting the exposome; thus, the genetic and epigenetic mechanisms that control or deregulate human physiology have also been affected. For example, the overgrowing use of plastics, and the chemicals derived, have been shown to promote disease by modifying epigenetic patterns. Moreover, fossil resources are finite, and thus, the dependence on these for such a large part of everyday activity is not sustainable. These facts led to 21st century scientists turning towards technologies with a small environmental footprint. These technologies range from the use of materials of biological origin in everyday products to biofuels and biobatteries for energy consumption (Table I). What characterizes such technologies is

Table I. List of traditional chemical products and their corresponding alternatives.

Currently used product	'Green' alternatives
Petroleum-derived industrial solvents	Alcohols (1-butanol, octan-2-ol, propane-1,3-diol), Ethyl lactate
Petroleum-derived lubricants	Natural vegetable oils (rice bran oil, rapeseed oil, coconut oil)
Non-biodegradable petroleum-derived plastics	Bioplastics (polycaprolactone, polybutylene succinate, polybutylene adipate, polylactic acid, polyhydroxyalkanoates, succinic acid, 1,3-propanediol based polymers, cellulose, starch, biobased polyethylene terephthalate, biobased polyethylene)
Fossil fuels	Biofuels (bioethanol, biomethane, biodiesel, biobutanol)
Batteries (alkaline and lithium-based)	Biobatteries (microbial fuel cells)

Table II. Advantages and disadvantages of the use of traditional chemical products and bio-materials.

	Advantages	Disadvantages
Chemical products	Already existing technology allows mass production Cost-effective	Harmful to the environment Harmful to human health Finite resources
Biomaterials	Eco-friendly Little to no harmful effects on human health Renewable resources	More research required for mass and safe production Expensive products Large initial investment needed

that their promise of 'greener' alternatives is not an easy task, even though the raw materials used are renewable natural resources. The majority of the occurring issues amount to the complex mechanisms through which a product can influence the environment since, at times, the current production process may be very energy-intensive and may thus provide no actual benefit against fossil-based products. Another issue is the economic viability of a product. The majority of 'green' alternative production processes require large investments, and the end-product may be costly. These differences in advantages and disadvantages (Table II) between 'traditional' products and their 'greener' alternatives are the reason why ecofriendly products are yet to surpass the production and the use of products harmful to both the environment and human health. Thus, further research is required to develop products that are both cost-effective, safe for use, and their entire production process is environmentally friendly.

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Authors' contributions

All authors (EP, TM, KD, AE, FB, GPC, EE and DV) contributed to conceptualization, writing, drafting, revising, editing and reviewing of the manuscript. All authors confirm the authenticity of all the raw data. All authors have read and approved the final manuscript.

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Competing interests

GPC is the Editor in Chief of the journal, and DV and EE are Editors of the journal. However, they had no personal involvement in the reviewing process, or any influence in terms of adjudicating on the final decision, for this article. The other authors declare that they have no competing interests.

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