Perspectives

Are ~~we~~ Controlled Release Scientists D~~d~~oing E~~e~~nough for O~~o~~ur E~~e~~nvironment?

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1. The Year 2020 - A turning point

2020 will go down in our collective minds as a year that seemed like things could not get worse, and then they got worse. So many catastrophic events seemed to occur worldwide that we, as a global community, may have become numb to the many environmental concerns that have become critical for our future existence on earth. During that challenging year, we focused on staying safe, protecting our loved ones, and doing what we could to beat a pandemic caused by the SARS-CoV-2 virus that causes the serious life-threatening disease known as COVID-19. This led us to focus more internally than externally, and rightfully so. The concept of putting your own oxygen mask on before attempting to help others was logical and appropriate. As we see vaccines and promising therapies to thwart the impact of this pandemic on the horizon, it may be the time to consider redirecting our focus onto other issues that affect our daily lives. While there are many options and opportunities for such focus, the goal of this Perspective article is to highlight the need and potential for allocating some of our collective efforts toward environmental issues.

2. Global warming

In 2015, the United Nations General Assembly adopted a resolution pursuing 17 goals by 2030 [1]. Goal 14 is to conserve and sustainably use our oceans, seas, and marine resources for sustainable development. It is followed by Goal 15, which is to protect, restore, and promote sustainable use of terrestrial ecosystems, sustainably manage forest, combat desertification, halt and reverse land degradation, and stop biodiversity loss. These two goals may be out of reach if we do not take immediate steps to change our current course of environmental mismanagement.

Let’s start with global warming. Yes, it is real, despite efforts by many to claim it is not and to point the blame away from man-made causes [2]. There are several implications of global warming that will affect some of the current efforts being made by scientists using controlled release technologies. For example, altered weather patterns associated with global warming have been correlated with increases in allergic diseases [3] and even the frequency of some urologic conditions [4]. And this is probably just the tip of the proverbal iceberg. Modeling studies have suggested that global warming will increase the frequency of vector-borne diseases like malaria, leishmaniasis, meningococcal meningitis, viral encephalitis, dengue, and chikungunya in the coming years and beyond [5]. Controlled release technologies have already been used to address many of these issues. For example, a DNA nanoparticle approach for gene therapy was shown to prevent airway remodeling in experimental allergic asthma [6]. Also, a zero-order controlled release of ciprofloxacin-HCl from a reservoir-based, bioresorbable, and elastomeric device was shown as a promising approach to treating certain urological conditions [7]. Additionally, a synthetic nanovaccine approach demonstrates feasibility for vector-borne disease prevention and therapy [8]. These are just a few examples showing how scientists using controlled release technologies have made significant contributions in areas that are likely going to worsen due to global warming. However, such efforts are only an indirect approach to cope with the inevitable increase in our planet's temperature.

The question to pose for the field is whether controlled release technologies can be used in ways to directly address some of the environmental issues we are currently facing as a global society. For example, consider how the increased temperatures and shift in moisture patterns have driven the spate of catastrophic storms worldwide as well as more extended, more devastating brush fires across most of Australia and forest fires in the western United States. Removal of water-capturing vegetation caused by these fires has led to more significant and wide-spread mudslides once rains finally arrive. Could controlled release technologies be used to improve fire retardants to reduce the extent of fire damage? Studies have shown that the diversity achieved through natural forest regrowth has a better outcome from natural processes compared to single species tree-planting efforts concerning carbon capture [9]. Could controlled release technologies be used to improve the pace of these natural reforestation processes, accelerating the establishment of the various ecosystems that are critical for the generation of a sustainable forest? Progress in these areas would involve controlled release scientists establishing new partnerships with experts in firefighting, botany, ecology, plant biology, forest management, etc.

Approaches to address environmental changes that result in increased forest destruction is just one facet of global warming. Other areas of the environmental disaster that we face could be considered for novel uses of controlled release technologies. There are six different kinds of forests: equatorial moist evergreen or rainforest, tropical deciduous, Mediterranean, temperate broad-leaved deciduous and mixed, warm temperate broad-leaved deciduous, and coniferous. Each forest type will require a distinct approach to encourage a desired biodynamic growth outcome. Could we take the next step with these approaches to identify controlled-release fertilizers and soil microbes optimized for these various types of reforestation efforts? Such efforts reflect an historic strength of controlled release scientists who have published in this Journal [10-12]. Finally, modeling can be used to predict the properties and performance of different controlled-release fertilizers [13], and efforts to use new materials, from modified cellulose to the generation of time-release fertilizers, are being explored [14]. Can we do more?

3. The plastic pollution

Plastic has been a significant part of the global climate crisis, and whether we are aware or not [15], it has had a direct impact on the health of the planet. The oceans have become a waste deposition site, with plastic waste being a primary culprit [16]. Microplastics and nanoplastics have been found at alarming levels from the depths of the ocean to Arctic ice and even inside our bodies [17-22]. We have been consuming micro/nanoplastics in the air, food, and water [23, 24].

Each of us is estimated to ingest 20 kg of plastic in our lifetime [25]. Americans appear to eat and inhale over 70,000 plastic particles each year [26], presenting severe concerns for human health [27]. Micro/nanoplastics are transported through the rain and water cycle, ending up in our local environments [28, 29]. Microfibers, mainly resulting from washing our clothes composed of synthetic polymers, have been found in all corners of the globe [30]. Plastic pollution has become a major issue for the planet's survival, being called the "plastic pandemic" [31]. Thus, the world currently has two pandemics, one deadly on a rapid time scale and another that is killing us in slow motion.

While recycling efforts have been successful and have somewhat improved the situation, a recent study suggests that ~80% of plastics still end up in the environment [32]. The hard-fought progress made in this environmental repair effort has made a significant retreat in the age of COVID-19. All efforts to reduce single-use plastic materials are on hold. In the COVID-19 environment, a significant portion of plastic wastes involves disposable medical items, including face shields, masks, syringes, etc. Can controlled release technologies be used to find solutions to the challenge of using biodegradable materials that could replace a large fraction of the medically-related plastic waste that ends up in our oceans and landfill? It is difficult to even put this level of concern into a perspective that can be readily appreciated. For example, between 920 million and 1.7 billion injections were performed using disposable syringes in the United States in 1998 alone [33]. Now, think of that number, increasing every year, since 1998 and into the future. Summing these numbers are staggering. Based on that limited information, it is difficult to even imagine the level of plastic personal protective equipment and treatment materials discarded during this period of COVID-19. Any efforts to produce biodegradable plastics that could diminish the environmental burden of this medically related plastic waste would have a massive impact on helping the environment.

Despite what seems like an obvious benefit from investing in biodegradable materials to replace plastics, some have questioned whether this is a realistic endeavor [34]. The major challenges involve scalable processes and cost of goods, but ther~~s~~e is hope. Biodegradable plastic approaches have been described, such as various polyester-based that can be degraded by various microorganisms [32]. Bacterial polyhydroxyalkanoates have also been investigated; these can be produced by Pseudomonas species or recombinant *Escherichia coli* strains, exhibiting thermoplastic and elastomeric properties that make them an attractive replacement for non-degradable plastics [35]. Seaweed polysaccharides, such as alginate and carrageenan, have also been proposed for bio-based plastic replacements [36]. Poly(lactic acid), polyhydroxybutyrate, polyhydroxyoctanoate, poly(butylene succinate), thermoplastic starch, polycaprolactone, and blends thereof have been described and tested for biodegradation in managed and unmanaged environments, with some promising results [37]. Ultimately, it will be essential to consider the role of microorganisms and their enzymes involved in the biodegradation of these polymers and the ecotoxicological impact of degradation products on soil microbial community and biogeochemical cycles [32, 38, 39].

The challenges discussed here are on a phenomenally large scale: in 2015 alone, 407 million tons of plastic were produced [40]. We need to consider how to replace them with biodegradable materials that can be prepared cheaper and on a larger scale than ever before. Here, controlled release scientists could set up new partnerships with engineers having expertise in scaling processes on a vast scale. Should we consider re-tooling derelict oil refineries into hydrocarbon-based biodegradable polymers? Can algae be used to capture CO_2 directly into a format that can be used for the preparation of degradable polymers? Controlled release scientists are very familiar with biodegradable polymers, as they have developed dozens of non-toxic, injectable, long-acting formulations. They are also highly competent in synthesizing new biodegradable materials. It is critical to note, however, that the real solution to the current plastic pandemic is not merely making new biodegradable plastics. These materials need to degrade promptly, e.g., a matter of months, not decades. More importantly, they should be produced at costs low enough to compete with non-degradable plastic alternatives.

4. Why us?

Controlled release scientists are extremely creative. They are genuinely passionate about what they do. Their plethora of contributions have already had a significant impact on the world to make it a better place in many ways. These contributions, however, are only a few of the many possibilities in which controlled release technologies could be applied. We have listed some of the obvious, current challenges we face as the human race continues to traumatize the earth with an ever-increasing population burden. There are many current issues that could be addressed now and other issues that will become critical in the future that will need to be considered. Expanding the impact of controlled release technologies beyond what they are currently being considered just might help save the world as we know it. No one knows these controlled release technologies better than the scientists who have thought of them and developed them for various applications. To achieve environmental benefits, we need to start concerted efforts to direct available resources toward studying topics that improve our life-knowledge rather than just paper-knowledge. Publishing research results is what we do, but research for the sake of publishing may not bring the knowledge and technology that society needs to deal with the challenging problems facing us today.

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