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Next-generation enhanced efficiency fertilizers for sustained food security

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Editor's summary

Conventional nitrogen fertilizers are costly for human and environmental health. This paper discusses the barriers and opportunities for designing enhanced efficiency fertilizers and incorporating these alternative technologies into policy and decision making.

Abstract

Nitrogen (N) losses in agricultural systems can be reduced through enhanced efficiency fertilizers (EEFs), which control the physicochemical release from fertilizers and biological N transformations in soils. The adoption of EEFs by farmers requires evidence of consistent performance across soils, crops and climates, paired with economic advantages. Here, we show that EEFs' benefits due to avoided social costs of N pollution considerably outweigh their costs – and must be incorporated in fertilizer policies. We outline new approaches to the design of EEFs using enzyme inhibitors with modifiable chemical structures and engineered, biodegradable coatings that respond to plant rhizosphere signalling molecules.

Main

A global population of 10 billion people will need to be fed by 2050[1]. Synthetic nitrogen (N) fertilizers are used for producing half of the world's food supply but less than half of the applied fertilizer N is utilized by crops and pastures[2,3]. The remaining N is lost to the environment via ammonia (NH_3) volatilization, nitrification, nitrate (NO_3^-) leaching, denitrification and runoff[3]. Nitrogenous fertilizer losses have contributed to environmental and ecological problems at regional and global scales: eutrophication, air and water pollution, biodiversity loss, climate change, stratospheric ozone depletion as well as damage to human health[4,5]. For example, elevated N input has caused an average decline of 16% in the herbaceous plant species richness in terrestrial and wetland ecosystems worldwide[6]. About 70% of the global population has been exposed to above-recommended levels of NO_3^- in airborne aerosols, water or food[7].

To ensure food security for the world's growing population without further threatening the planet's health, the efficiency of N fertilizers needs to be increased significantly. Management practices like the 4R Nutrient Stewardship strategies (right source, right rate, right time, and right place) can help to reduce N losses from agricultural production systems[8]. A better synchrony of fertilizer N supply with crop demand can be achieved through improved fertilizer technologies, in particular enhanced efficiency N fertilizers (EEFs) that increase the technical and economic efficiency of N fertilizers. Fertilizer efficiency-enhancing products include: (i) urease inhibitors, which suppress the activity of the enzyme urease and lower the rate of urea hydrolysis, thereby decreasing NH_3 emissions[9]; (ii) nitrification inhibitors, which slow down the microbial conversion of NH_3 to nitrite (NO_2^-) and consequently to NO_3^-, reducing the risk of nitrous oxide (N_2O) emission, NO_3^- leaching, and denitrification[10]; and (iii) controlled-release fertilizers, where a physical barrier or polymeric coating regulates the release of N depending on external stimuli such as soil moisture, pH and temperature, thereby synchronizing plant N demand and fertilizer N supply while minimizing N losses from multiple pathways[11]. EEFs are expected to maintain N in the root zone, which increases N availability to crops and decreases N losses to the environment, thus providing an opportunity to reduce fertilizer N input (in proportion to the amount of 'saved' N) without compromising productivity.

The development of inhibitors (urease and nitrification) and controlled-release coatings started more than 50 years ago[12]. Currently, potential candidates for inhibitors are commonly identified through computationally random screenings of large libraries of commercially available chemicals. This non-systematic approach prevents breakthroughs because it does not address the specific limitations of the existing inhibitors, such as highly variable and unpredictable performance in different soils, in addition to volatility and chemical instability, which will likely become an even more pressing problem under future warmer climates[9,13]. A range of natural and synthetic materials have been developed as controlled-release coatings, but these are costly, may be toxic to the soil environment, non-degradable, or crack easily[14,15]. Furthermore, the release kinetics of these coated fertilizers is neither well understood for specific edaphic or environmental conditions nor directly responsive to the nutrient demand of plants.

The currently available EEFs are not widely adopted by farmers who do not see them as economically attractive alternatives. Farmers traditionally consider input costs *versus* expected benefits when making decisions about using fertilizers to grow crops and pastures[16]. However, there are further costs arising from N losses from agricultural production systems that are unintended and uncounted in the decisions of the producers and consumers. These external, or social costs pertaining to ecosystem and human health reduce the welfare of people in society[5,17]. The social cost of N pollution is defined as the present value in monetary terms of the damage caused by losses of N to the environment[17]. Estimates of social costs of N pollution for regions have been made[18,19,20]. For example, the annual total social cost of agricultural N losses arising from damage to human health and ecosystems as well as changes to the climate was €40−230 billion for the European Union (27 member states, EU27) in 2008[20]. In the US, the total annual health and environmental damage of anthropogenic N was estimated to amount to US$81–441 billion per year in the early 2000s[18]. A preliminary estimate of the global damage cost associated with N pollution is US$200−2000 billion each year[19]. As the magnitude of total social costs arising from losses of N from agricultural systems are large, using EFFs to abate these losses holds the promise of substantial social benefits that should be incorporated into fertilizer decision and policy making.

In this Perspective, we outline the potential for EEF technologies to reduce N losses, propose new multidisciplinary approaches to design of EEFs, and advocate the incorporation of social costs of N pollution into fertilizer decision making and public policy.

EEFs reduce N losses and social costs

Figure 1 summarizes the results of 21 meta-analyses (published prior to July 2021) on the potential of EEFs to reduce N losses from food production systems, at both regional and global scales. The data show that, relative to conventional fertilizers, NH_3 emissions were 50–74% lower (range of the mean reduction) when urease inhibitors were used, whereas N_2O emissions were either unaffected or decreased (28–49%). When nitrification inhibitors were used, N_2O emissions, N leaching and N runoff were decreased by 27–58%, 17–58% and 45%, respectively, but NH_3 emissions were unaffected or increased by 13–52%. When formulations combining both urease and nitrification inhibitors were used (double inhibitors), emissions of NH_3 and N_2O were decreased by 36–75% and 30–50%, respectively, whereas N leaching ranged from –51% to +58%. When controlled-release fertilizers were used, NH_3 emissions, N_2O emissions, N leaching and N runoff were decreased by 27–83%, 8–77%, 17–92% and 32%, respectively.

INSERT FIGURE 1 ABOUT HERE

These data clearly demonstrate that EEFs can reduce N losses from agricultural systems to a certain degree. Thus, considering the immense damage costs per unit of N pollution (e.g., in the EU27, €2−20/kg N for NH_3 emissions damage to human health; €4−17/kg N of N_2O emission to climate; and €5−20/kg N for N deposition and leaching to ecosystem eutrophication and biodiversity loss)[20], EEFs offer a huge potential for decreasing the social costs of N pollution. While there are geographical differences in the avoided social costs, there will be substantial benefits particularly for regions with higher risk of human and ecosystem exposure to N pollution. The wide range of responses shown in Figure 1 suggests that the performance of a particular inhibitor or coating is not universal; the expected benefits of EEFs are not always achieved in all soils, climatic conditions or agricultural systems. The variation in the performance of EEFs with soil texture (Supplementary Fig. 1), climate zone (Supplementary Fig. 2) and crop species (Supplementary Fig. 3) highlights the need to improve the capability of EEFs to further reduce N losses and associated social costs across regions and diverse agricultural settings.

New approaches to EEF design

At present, the development and improvement of existing EEFs largely relies on expertise in agronomy and soil science that informs crop phenology, root architecture and N demand over the growing period, as well as N supply with respect to soil physical, chemical and biological factors. However, to achieve a major breakthrough in the design and development of more efficient inhibitors and coatings that are able to target diverse soils, climates and crops, a multidisciplinary approach is needed that integrates agronomy and soil science with synthetic chemistry, chemical engineering, plant physiology and plant biochemistry.

Inhibitors

Urease inhibitors and nitrification inhibitors target the soil enzymes urease and ammonia monooxygenase (AMO), respectively (Fig. 2a). Presently, three urease inhibitors (dominated by *N*-(*n*-butyl) thiophosphoric triamide (NBPT))[9] and several nitrification inhibitors (dominated by 3,4-dimethylpyrazole phosphate (DMPP), dicyandiamide (DCD) and nitrapyrin (N-serve)) are commercially available[21]. Inhibitor performance is currently improved by modifying fertilizer formulations using the existing inhibitor compounds based on the findings of degradation studies on inhibitors and microbiological studies on soil urease and AMO. However, this approach does not overcome the major impediments of these inhibitors, such as limited stability, volatility and a highly variable inhibitory efficiency in different soils[9,13]. To improve the inhibitor performance under diverse agricultural and environmental settings to further reduce N losses and associated social costs, a new approach is required that involves the systematic design and testing of new molecules to specifically address the known or anticipated obstacles hindering the effectiveness of the inhibitors. Strategies similar to those used in the pharmaceutical drug development process[22] should be adopted, such as the discovery of lead compounds through structure-activity, molecular docking and degradation studies[23,24]. These can then be further modified to improve efficiency and reduce undesired side effects, such as insufficient stability and residence times in soils. This approach, in conjunction with investigations of the interactions between inhibitors, fertilizers and the soil-root-microbe system, can be applied to develop efficient inhibitors with sufficient longevity and which are synthetically accessible on an industrial scale. Examples of new designs to existing urease and nitrification inhibitors are given below.

Urease inhibitors

Many compounds with urease inhibitory activity are known, which vary considerably in structure, size and mode of action[25]. NBPT is the most commonly used commercial urease inhibitor in agricultural systems. It is a urea analogue, which, following conversion into *N*-(*n*-butyl) phosphoric triamide (NBPTO) in aerobic soils, binds in the active site in urease and slows down urea hydrolysis, thereby reducing NH_3 volatilization[9]. However, both NBPT and NBPTO undergo microbiological and hydrolytic degradation in acidic and slightly alkaline soils, causing the rapid loss of inhibitory activity[9]. Strategies for improving urease inhibitors will address their stability towards hydrolytic decay, which needs to be suppressed to reduce unwanted losses of NH_3. In the case of NBPTO, for example, increasing the steric bulk around the P=O moiety or lowering the electrophilicity of the central P atom to reduce or prevent attack by water could be strategies to slow down hydrolytic decomposition of the inhibitor. Furthermore, laboratory studies have shown that the inhibitor-enzyme interaction and therefore inhibition efficiency can be increased by replacing the lateral *n*-butyl group with substituents (R) that provide an additional binding site[26]. Another disadvantage of NBPT is its relatively short active period at higher soil temperatures[9].

Recently, *N*,*N*'-disubstituted acylthioureas have shown potential as urease inhibitors with increased temperature tolerance[27], providing opportunities to improve their inhibitory performance through variation of the substituents R (Fig. 2b).

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Nitrification inhibitors

DMPP is a popular nitrification inhibitor because of its low application rate, low ecotoxicity, and generally perceived high efficiency[13]. 3,4-Dimethyl-1H-pyrazole (DMP) is the actual inhibitor, which is volatile and commonly 'fixed' as phosphoric acid salt to reduce loss through evaporation. Newer approaches to lower the volatility of DMP-based inhibitors in soils involve derivatization of DMP with succinic acid, but this product is currently not used commercially[28]. When DMPP-coated urea fertilizer is applied, it is possible that the highly soluble urea rapidly distributes in soils whereas the positively charged DMPP could be adsorbed on negatively charged soil colloids, affecting its movement along and across the soil profile. This mismatch could lead to the spatial separation of fertilizer and inhibitor that might reduce or eliminate inhibitory efficiency. Furthermore, the effectiveness of DMPP can drastically decrease with increasing soil temperature[29]. Degradation in the soil could also contribute to the variable inhibitory performance of DMPP. In fact, the loss of DMPP from soils was shown to follow first-order kinetics with a half-life varying between 5 and 28 days[30]. We recently found that DMPP undergoes degradation in soils through chemical processes, possibly involving reactive oxygen species formed through abiotic and biotic pathways, which results in side-chain oxidation and dimerization[31]. Ammonia monooxygenase (AMO), the enzyme targeted by nitrification inhibitors, loses its structural organisation and function upon isolation, preventing detailed studies of the active site. It is known that copper (Cu) and possibly iron (Fe) are involved in the enzymatic functionality, indicating that nitrification inhibitors might inhibit AMO through complexation of the Cu centre[32]. The development of improved nitrification inhibitors will require detailed structure-activity relationship (SAR) studies, where compounds with different properties are systematically screened. For example, increasing the molecular weight of the pyrazole using slightly larger or additional substituents, such as groups that form hydrogen bonds or allow electrostatic interactions with soil components, will lower the volatility of the substrate. Other cyclic or acyclic compounds with heteroatoms that strongly coordinate with Cu, such as N, oxygen or sulfur, could provide structural motifs that invite manipulation of the molecular properties through different substitution patterns, thereby providing the opportunity to tailor the operational inhibitor performance for specific soils and environments (Fig. 2b). We recently demonstrated that readily accessible 1,2,3-triazoles with short non-polar substituents can outperform DMPP in neutral soils at 35°C[33].

Controlled-release coatings

Recent reviews have comprehensively summarized the strengths and weaknesses of various natural and synthetic coating materials used as controlled-release fertilizers[14,15]. Polymer-based materials are well-suited fertilizer coatings because the surface properties, such as mechanical strength and surface reactivity, are easily modified. However, the use of these products has been constrained by high costs, complicated synthesis procedures and non-biodegradability[14,15]. Research frontiers have shifted towards materials that are environmentally benign, such as bio-oil (fatty acid-based oil), and naturally occurring polysaccharides including cellulose, chitin, starch, lignin, and materials such as polylactic acid[34] and metal phenolic networks[35]. Polysaccharides and polyphenols are of particular interest as they are relatively inexpensive and can offer tuneable porosities, via swelling mechanisms, and surface functional groups that can aid in controlling the release of the encapsulated fertilizers. Recently, urea granules have been encapsulated within liquid marbles[34], which are microspheres of fluid droplets coated by hydrophobic powders[36]. With this polymer technology, water permeation rates into the capsule can be controlled via manipulation of the pore size of the polymer film coating. This design feature allows the dissolution of nutrients and their migration through the film to be tailored for agricultural soils in diverse rainfall zones. The functional groups on the surface of liquid marbles may be modified such that the material dissolution can be triggered to release the encapsulated fertilizers in response to external stimuli including pH, ionic strength, ultra-violet radiation and temperature[37]. This polymer technology opens up opportunities for targeted nutrient release to the soil environment of specific agricultural systems.

Existing controlled-release coatings have been designed to meet the predicted needs of plants for nutrients, but they do not respond directly to plants' real-time nutrient demand or plant-soil microbe interactions. We propose a plant-oriented approach to developing a new class of controlled-release coating that harnesses rhizosphere microbes to facilitate nutrient acquisition. The plant-microbe complex comes into play, which involves below-ground two-way communication, mediated by signalling molecules such as proteins, peptides, lipids, small RNAs, phytohormones, and metabolites[38,39]. Many studies have demonstrated that specific groups of microbiota are persistent and ubiquitous in the rhizosphere of a particular host plant[40,41] and are functionally important for the fitness of the plant[42,43]. Plant rhizosphere microorganisms use chemotaxis, i.e., the movement in relation to the concentration gradient of a chemical stimulus, to sense and respond to plant signalling molecules (e.g., sugars and organic acids in plant root exudates)[44]. Once a plant signal for nutrient uptake is perceived, microbes attach to the root surface, form a biofilm, and assist host plants to acquire nutrients[44]. In this regard, high-throughput metabolomic technologies[45] enable identification and selection of crop-specific plant signalling molecules that promote activities of N-cycling microbes and benefit plant N uptake. Besides, signalling molecules can be selected to attract beneficial microbes in the rhizosphere that improve the resistance of a crop to drought, pathogens and diseases[44,46]. These signalling molecules can be incorporated into fertilizer coatings and, when released, would attract beneficial microbiota that promote N use efficiency for a range of crops (Scenario 1, Fig. 3). It is challenging to define and isolate these specific molecules from the complex soil matrix, but recent progress in synthetic biology allows targeted analyses of individual signalling pathways[47] and offers promising prospects for the exogenous application of signalling molecules in fertilizer technology. Another plant-oriented controlled-release coating is one that responds to plant signals for N acquisition such that N is released when needed by the plants. Plants interact with rhizosphere microbiota by releasing root exudates, the composition of which depends on various abiotic and biotic factors[48]. Progress has been made in demonstrating how plants sense and respond to the availability and distribution of external NO_3^- pools, and the signalling pathways involved in monitoring N status[49]. While NO_3^- possesses strong signalling effects on the architecture of the root system[50], root responses to NO_3^- are mediated by nitrate transporters such as NRT2 and NRT1, which modulate the transport of auxin, plant hormones and signal molecules to regulate root development[51]. Some crop plants such as sorghum, rice and wheat can release biological nitrification inhibitors, such as 1,9-decanediol (from rice), which regulate the microbial N transformation and improve N use efficiency[52]. The secretion of 1,9-decanediol by rice plants is triggered by environmental stimuli such as low to moderate NH_4^+ concentrations[53]. The secondary metabolites produced by plants under stress conditions act as signalling molecules to tailor the rhizosphere microbiome[54]. Recent structural studies have revealed the underlying mechanisms of how plant receptors perceive distinct signalling molecules and become activated[55]. We envisage that fertilizers can be coated or chelated by substances, e.g., receptors that respond to biological signals including root exudates (Scenario 2, Fig. 3), which trigger nutrient release for plant uptake when needed. The development of such fertilizer coatings requires a better understanding of the determinants of the rhizosphere microbiome composition and biochemical signals in the root exudates of targeted plant species, together with receptor–signalling molecule interactions.

INSERT FIGURE 3 ABOUT HERE

Outlook and policy implications

Fertilizers that are efficient both from the viewpoint of farmers and the wider environment and economy are destined to play a pivotal role in achieving global food security and environmental stewardship. The development of next-generation EEFs that are tailored for specific soils, crops and climates to optimize fertilizer N use will only be possible by integrating multidisciplinary expertise and technological advancement into fertilizer design and development. The benefits of EEFs would be maximized when used in combination with knowledge-based management practices such that conventional fertilizer N input is adjusted based on the ‘saved’ N with the use of EEFs to improve productivity and minimize N pollution[12].

Wide adoption of EEF technologies will hinge on the demonstration of net benefits to farmers[56], and effective information dissemination to farmers and their extended networks[57]. For example, it is worth noting that substantial increases in the transportation costs of EEFs relative to conventional fertilizers would not be expected because EEFs are in principle conventional fertilizers that are coated with a very thin and light layer of inhibitor compounds and/or polymers. Farmers can use the same fertilizer application equipment for EEFs as they do for conventional fertilizers, hence no additional machinery cost would incur. The carbon footprint of the production and transportation of EEFs remains similar to that of conventional fertilizers based on a life-cycle assessment[58]. Moreover, a global meta-analysis shows that the use of nitrification inhibitors does not increase methane emissions[59]. In regions facing crop failures and food shortages consequent on infertile soils, arid climates and insufficient N inputs (e.g., in sub-Saharan Africa), N policies tend to prioritize food production over N pollution mitigation[60]. Nonetheless, it is encouraging to note that controlled-release fertilizers are becoming more common in sub-Saharan Africa for growing high-value crops[61].

We advocate the identification and valuation of the social costs (i.e., adverse environmental and health impacts) caused by fertilizer-induced N pollution as essential steps to formulating policies that promote the development and use of EEFs. Regulations and penalties, or incentives to adopt EFFs such as taxes, tradeable rights, subsidies and credits, are ways of reducing the social costs of N losses[62,63], keeping in mind that these various policies vary in their effectiveness and sharing of the burdens and benefits. Policies to reduce the social cost of N pollution have regional, national and international implications, and will need to be cognizant of the stages of economic development of countries involved[60]. Opportunities further along the value chain are created as well[62]. As consumers' concern about environmental pollution and related health impacts continues to increase, the reduction in negative attributes resulting from reduced social costs due to enhanced N efficiency will broaden the appeal to consumers, and thus provide opportunities for food value chains that supply credibly differentiated low-N agricultural products, for example through creating environmental impact food labels[64] that inform consumers about the environmental friendliness of food products.

Prevention is better than cure. Establishing incentives to adopt EEFs to minimize N pollution at the source is by far a better strategy than cleaning up the pollution after it occurred, without guaranteed success and at higher costs.

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Contributions

S.K.L. and D.C. designed the study. S.K.L., U.W., H.H., F.C., K.M., X.L. and B.M. wrote the first draft and all authors contributed to the discussion and revision of the manuscript.

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Ethics declaration - Competing interests

The authors declare no competing interests.

Supplementary information

Supplementary Note 1, and Supplementary Figs. 1-3

Data availability statement

Data included are already published and publicly available, with those publications properly cited in references.