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Cost–benefit analysis of nanofertilizers and nanopesticides emphasizes the need to improve the efficiency of nanoformulations for widescale adoption

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Nanotechnology-based approaches have demonstrated encouraging results for sustainable agriculture production, particularly in the field of fertilizers and pesticide innovation. It is essential to evaluate the economic and environmental benefits of these nanoformulations. Here we estimate the potential revenue gain/loss associated with nanofertilizer and/or nanopesticide use, calculate the greenhouse gas emissions change from the use of nanofertilizer and identify feasible applications and critical issues. The cost–benefit analysis demonstrates that, while current nanoformulations show promise in increasing the net revenue from crops and lowering the environmental impact, further improving the efficiency of nanoformulations is necessary for their widescale adoption. Innovating nanoformulation for targeted delivery, lowering the greenhouse gas emissions associated with nanomaterials and minimizing the content of nanomaterials in the derived nanofertilizers or pesticides can substantially improve both economic and environmental benefits.

It is expected that demand for all types of crops will significantly increase in the coming decades to meet the crop demand of the expanding global population. While the production of wheat and rice has been increasing steadily over the past 70 years, the growth rate of vegetable, fruit, soybean and rubber tree production has increased at a faster pace (Fig. 1 and Supplementary Fig. 1).

The primary method used to increase crop yields—increased use of conventional fertilizers and pesticides—is no longer yielding the needed growth (suggested by the plateaued consumption of fertilizer and pesticide; Supplementary Fig. 2)[1] and has resulted in significant environmental damage, a result of over-application of fertilizers and inefficient uptake (for example, 30–35%, 18–20% and 35–40% of N, P and K fertilizer were uptaken by plants[2]; 10–70% of applied pesticides reaching plants[3] with possibly <0.1% reaching biological targets[4]).

The use of nanotechnology-based approaches for crop yield enhancement has demonstrated encouraging results[2,5], especially

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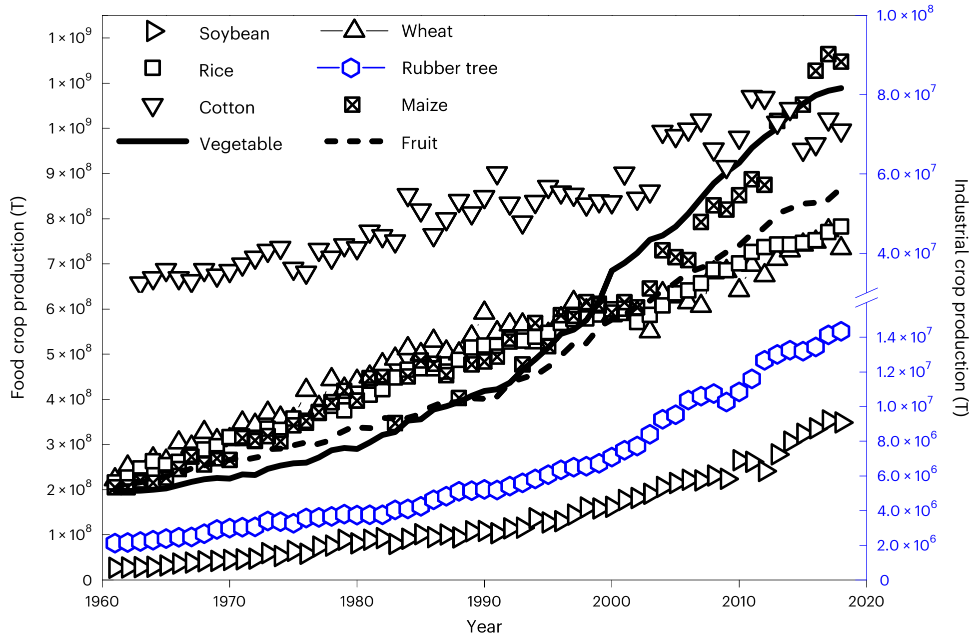

Fig. 1 | Guaranteeing the supply of fruit, vegetables and non-food crops while providing sufficient grains. On the basis of 2013 population and food consumption data, the production of wheat and rice will have to increase to 9.2×10^8 and 9.7×10^8 tonnes by 2050 (approximately 30% higher than their production in 2013) to satisfy global demand. However, the production of maize, vegetables (primary, that is, coming directly from the land and without undergoing further processing), fruits (primary) and rubber (an example of an industrial crop) will probably need to increase to meet global demand by 110%, 80%, 65% and 91%, respectively, on the basis of their 2018 production levels. Data of global crop production from 1960 to 2018 were collected from FAOSTAT (https://www.fao.org/faostat/en/#data/QCL).

in the field of nanofertilizers and nanopesticides[3,6–9]. Fertilizer compounds (for example, N, P and K) can be made into, and applied as, nanoparticles (NPs). Alternatively, inert NPs can be used as nutrient carriers (for both macro- and micronutrients) in agricultural practices[2]. Recent studies have demonstrated that multiple stages of plant growth benefit from the application of NP fertilizers (germination, growth, flowering and fruiting), and discussed the underlying mechanisms responsible for the increased plant production[2,10,11]. Nanofertilizers (that is, zerovalent iron NPs, ZnO NPs and nanomolybdenum) can also be used to remediate soil from contamination by pentachlorophenol, Cd, As and Cu (refs. [12–14]). In addition, nanofertilizers may contribute to the nutritional value of crops, which can alleviate certain nutrient deficiency diseases in humans (that is, Zn, Fe, Ca and Se deficiency)[15]. Owing to the high efficiency, it is possible that nanofertilizers can (partially) replace heavily dosed conventional fertilizers for growing nutrient-demanding crops, such as rice, wheat, apple, pear and grape[16,17]. However, it is unclear whether this increased production can offset the increased cost of NP-based fertilizers. Moreover, greenhouse gas (GHG) emissions from fertilizer synthesis and use account for a large portion of man-made GHG emissions. For instance, production of N fertilizer alone makes up approximately 2% of the world's energy consumption; about 60% of anthropogenic nitrous oxide release is mainly from microbial nitrification and denitrification of the residual fertilizer in croplands[18,19]. It remains unclear how the use of nanofertilizers could impact the overall GHG emissions from fertilizer synthesis and use.

Pesticides have been employed to treat a wide array of plant diseases. However, some endogenous (residing in a plant's conductive system) or exogenous (residing in intercellular spaces of plant tissues) pathogens can grow on or in leaves, stems, roots, fruits and seeds, making it hard for conventional pesticides to treat and causing a significant decline in crop yield. Recent advances in nanotechnology show that nanopesticides can be employed to replace conventional pesticides[20–22]. A wide range of nanoscale agents including pristine NPs (for example, nano-Ag, nano-CuO, nano-ZnO and nano-S_8^0) have been shown to be effective in inhibiting the growth of plant-associated bacteria and fungi, on the basis of in vitro experiments[21,23–25]. Different techniques can deliver NPs onto plants, leading to the enrichment of NPs at targeted tissue, such as leaves, trunks and roots[26–28]. Tuning the surface physicochemical properties (such as hydrophilicity, surface charge and polymer layer thickness) and size can potentially deliver and mobilize/immobilize NPs into plant cells, organelles and conductive systems (xylem and phloem, responsible for the upward and downward transport of water/nutrients, respectively), which allows NPs to combat both endogenous and exogenous pathogens[23,28]. However, it is unclear whether these nanotechnology-based approaches are economically feasible for combatting different crop diseases.

Adopting nanotechnology for non-food crop production is also very attractive as nanotechnology-based amendments can improve the desirable properties of the final products[29]. According to a 2008 study, 60% of the world's total harvested biomass was used for animal feed, 4% for material use and 4% for energy production[30]. Therefore, there is ample opportunity for nanotechnology to play an important role in agricultural practices. However, before nanotechnology is widely adopted, it is critical to carry out a cost–benefit analysis on the use of nanofertilizers and nanopesticides for growing different crops. In this analysis, we evaluate the potential revenue gain/loss (including the environmental cost of a fertilizer) associated with nanofertilizer and/or nanopesticide use, calculate the GHG emissions change resulted from the use of nanofertilizer and identify feasible applications and critical issues that need to be further explored.

Results and discussion

Cost–benefit analysis of nanofertilizers

Although not much information is available, there are several studies that allow us to perform a preliminary cost–benefit analysis of employing NP-based fertilizers and compare them with traditional fertilizers. In terms of macronutrients (that is, N, K and P), it remains largely unknown whether the use of nanofertilizers can generate net positive revenue,

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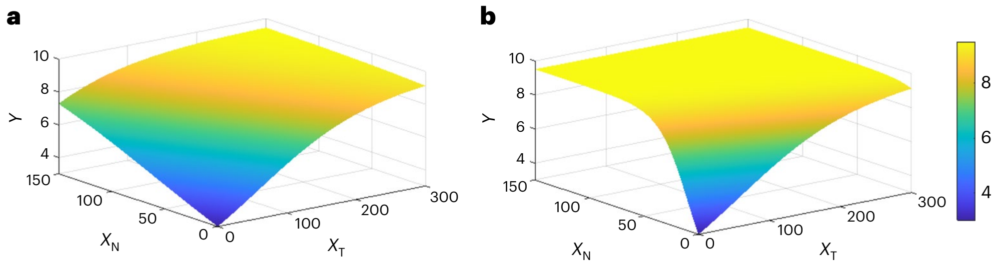

Fig. 2 | Efficient nanofertilizers can significantly reduce fertilizer dosage for the same corn yield compared with that of conventional fertilizers. Surface plot of corn yields (Y, t ha^{-1}) under different conventional fertilizer (X_T, kg ha^{-1}) and/or nanofertilizer (X_N, kg ha^{-1}) dosage: (a) $\gamma = 1$ and (b) $\gamma = 6$ ($\gamma = 3, 4, 5$ and 9 in Supplementary Fig. 3).

as well as how to apply nanofertilizers to achieve both economic and environmental benefits. Using K as an example, conventional K fertilizer use (1.33 g K per 15 kg soil) was found to increase corn yield (obtained from the control group without fertilizer) by approximately 16.7%, while the yield increase brought by a nanoformulated K varied between 9.5% and 24.5%, depending on the dosage (0.26 g to 1.33 g K per 15 kg soil)[31]. Given the unit price of a nanoformulation is higher than the conventional fertilizer, it is very likely that, for a given crop, there is an optimal dosage of nanofertilizers that maximizes revenue. In general, it has been reported that the application of nanofertilizers can increase crop yield by 10–30% (ref. [3]). Assuming a 20% yield increase, it is estimated that nanofertilizers can add (U.S. dollars) \$133.2, \$66.0 and \$86.4 ha^{-1} to the revenues from corn, wheat and soybeans, respectively (based on data from https://ag.purdue.edu/commercialag/home/paer-article/2018-purdue-crop-cost-return-guide/). In addition, because of the lower dosages of nanofertilizers needed to achieve enhanced growth and yields, the total cost of nano-N (typical dosage 10 kg ha^{-1}, cost \$100 ha^{-1}), nano-P (typical dosage 5 kg ha^{-1}, cost \$125 ha^{-1}) and nano-K (typical dosage 5 kg ha^{-1}, cost \$125 ha^{-1}) is estimated to be \$350 ha^{-1} (based on data from https://inscx.com/shop/), while that of conventional fertilizer for corn, wheat and soybean are \$296 ha^{-1} (270.0 kg anhydrous ammonia ha^{-1}, 79.9 kg P_2O_5 ha^{-1} and 81.0 kg K_2O ha^{-1}) \$200 ha^{-1} (123.8 kg urea ha^{-1}, 64.1 kg P_2O_5 ha^{-1} and 59.6 kg K_2O ha^{-1}) and \$116 ha^{-1} (0 kg N ha^{-1}, 38.2 kg P_2O_5 ha^{-1} and 90.0 kg K_2O ha^{-1}), respectively (based on data from https://ag.purdue.edu/commercialag/home/resource/2020/03/2020-crop-cost-and-return-guide/). It is currently unclear whether it is economically beneficial to replace some or all of conventional fertilizers with nanofertilizers. Importantly, the substitution may have significant environmental benefits because of the lower dosages needed of nanofertilizers. These benefits can stimulate the adoption of nanotechnology in agricultural practices.

Herein we use maize and N fertilizer as an example to quantitively estimate the economic and environmental benefits associated with nanofertilizer use. As illustrated in Fig. 2, in the absence of nanofertilizers (control group), corn yields gradually increase from 4.1 t ha^{-1} to 9.5 t ha^{-1} when conventional fertilizer dosage (X_T) increases from 0 kg ha^{-1} to 300 kg ha^{-1}. Notably, when the dosage is higher than 150 kg ha^{-1}, increasing dosage does not substantially increase yield, suggesting an increasing waste of fertilizer at high dosages. In terms of nanofertilizers, different γ values (relative efficiency of the nanofertilizer to traditional one, defined in Methods) result in different crop yields. By increasing γ from 1 to 9 and considering a nanofertilizer dosage between 0 kg ha^{-1} and 50 kg ha^{-1}, the yield increases significantly (Fig. 2 and Supplementary Fig. 3). For example, compared with the dosage of conventional fertilizer (200 kg ha^{-1}) needed to obtain a high yield (>8.0 t ha^{-1}), a much lower dosage of nanofertilizer is needed (40 kg ha^{-1}) with $\gamma = 6$. Moreover, it may be feasible to combine conventional and nanofertilizers as a co-dosing approach to increase yield even further (Fig. 2), which is currently widely explored, for example, co-dosing fertilizer with carbon-based nanomaterials[32–34]. The benefit of the co-dosing method is that it lowers the total cost of fertilizer application (through the use of conventional fertilizers) while increasing the yield (through the use of the nanofertilizers). However, it is worth noting that both X_T and γ can impact the increased rate of yield significantly. For instance, the increase in corn yields within a range of 0 kg ha^{-1} to 50 kg ha^{-1} of nanofertilizers with $\gamma = 6$ is much higher than that with $\gamma = 1$ or 4 (with the same X_T); increasing X_T from 50 kg ha^{-1} to 150 kg ha^{-1} can reduce the rate of yield from the increased usage of nanofertilizers (with the same γ) (Fig. 2 and Supplementary Fig. 3). In sum, nanofertilizer with a high γ value can efficiently increase crop yields and reduce fertilizer dosage significantly, which will be beneficial to the environment.

While applying nanofertilizers can significantly increase crop yields, the current price of nanofertilizers is still much higher than that of conventional fertilizers. As the overall cost of fertilizers has a linear relationship with dosage for both conventional and nanofertilizers, high dosage leads to a large cost discrepancy between conventional and nanofertilizers. Therefore, it is essential to estimate the revenue change after adopting nanofertilizers. Through equations (2–7), revenue under different scenarios was calculated (Supplementary Fig. 4) and the maximum revenue was determined (Fig. 3). Excluding environmental costs from the cost–benefit model, the observed 'revenue' under the recommended conventional fertilizer dosage (180 kg ha^{-1}, without nanofertilizer) is \$864 ha^{-1} (Fig. 3). However, after including environmental costs into our model (without nanofertilizer), a maximum revenue of \$475 ha^{-1} is obtained with a dosage of 49 kg of conventional fertilizers per hectare (Fig. 3); this finding implies that there is a large environmental cost under the high-dosage scenario using conventional fertilizers.

In terms of nanofertilizers, when γ is ≤2 (Fig. 3), the maximum revenue (subtracting environmental costs) is obtained when no nanofertilizers are used (\$475 ha^{-1}), indicating that at these γ values nanofertilizers do not generate positive net revenue under the assumptions made in our model. However, lower unit prices, less N leaching and higher N use efficiency can lower the critical γ value under which positive net revenue can be generated by using nanofertilizers. In the current model, when γ increases to 3, co-dosing 49 kg ha^{-1} conventional fertilizers and 24.5 kg ha^{-1} nanofertilizers generate a maximum revenue of \$510 ha^{-1} (Fig. 3). When γ further increases from 4 to 9, the maximum revenue increases from \$649 ha^{-1} to \$982 ha^{-1} while the optimal dosage of nanofertilizers declines from 42 kg ha^{-1} to 28 kg ha^{-1} (Fig. 3). That is, nanofertilizers with a high γ value are able to completely replace conventional fertilizer and generate higher revenues, while those fertilizers with medium γ values (that is, $\gamma = 3$) should be used to partially replace conventional fertilizers (which is the current stage of the research in this field). Notably, with highly efficient nanofertilizer ($\gamma = 9$), the maximum revenue (\$982 ha^{-1}; Fig. 3) is even higher than the observed revenue with only conventional fertilizer at the recommended dosage (\$864 ha^{-1}, without taking environmental costs into consideration), indicating highly efficient nanofertilizers can significantly increase

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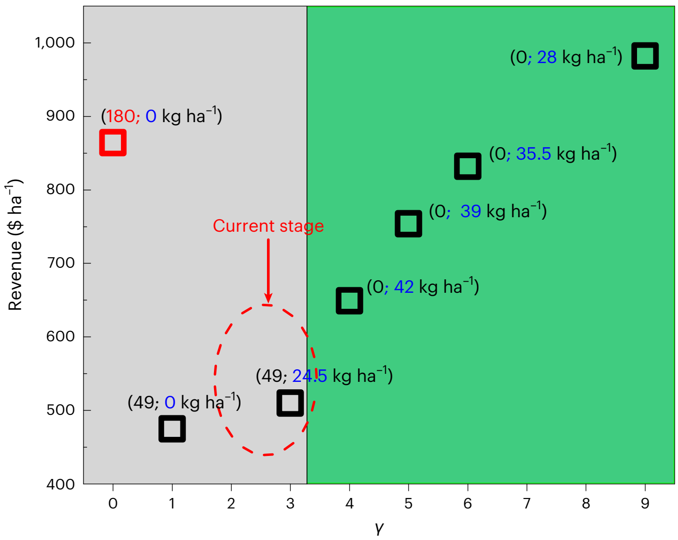

Fig. 3 | Maximum revenue under different fertilizers dosage schemes (X_T; X_N kg ha^{-1}). These data were obtained by plotting the maximum values of the curves obtained in Supplementary Fig. 4. The grey zone on the plot represents partial replacement of conventional fertilizer with nanofertilizer, while the green zone represents full replacement of conventional fertilizer with nanofertilizer. Red square marks the maximum revenue using only conventional fertilizers without taking environmental cost of fertilizer into consideration, while the black squares represent the maximum revenue after subtracting environmental costs; black numbers signify conventional fertilizer dosage; blue numbers signify nanofertilizer dosage.

the yield while lowering the environmental impact in comparison with that brought by conventional fertilizers. However, current data from the majority of studies on nanofertilizer indicate that the efficiency of nanofertilizers largely remains below 3, and more work on composition optimization needs to be done. In addition, in the co-dosing scenario, it is worth investigating how to use nanofertilizer efficiently along with conventional fertilizers.

In addition, among all the micronutrients, zinc is critical for plant growth. In a recent study[35], zinc was delivered by spraying 16 l of 10 mg l^{-1} nano-ZnO (nZnO) suspension per hectare, which increased pearl millet yield by 37.7%. While the cost of nZnO fertilizer ($0.0048 ha^{-1}) is more than an order of magnitude higher than that of conventional (that is, non-nano) ZnO ($0.00032 ha^{-1}), the net revenue increase by using nZnO is estimated to increase from $38.6 ha^{-1} (using conventional ZnO) to $103.1 ha^{-1} in India (commodity price of pearl millet, $25.65 per 100 kg; https://www.commodityonline.com/mandiprices/bajra-pearl-milletcumbu). Another case study investigating nano-Fe_2O_3 (nFe_2O_3) fertilizer showed that the use of nFe_2O_3 fertilizer (50 mg Fe kg^{-1} soil, or 20 kg nFe_2O_3 ha^{-1}) increased tomato yield from 22.6 t ha^{-1} (without Fe dosage) to 59.2 t ha^{-1} while 100 mg conventional Fe ($FeCl_3 \cdot 6H_2O$) or chelated Fe per kg soil increased yield to only 29.3 t ha^{-1} and 35.5 t ha^{-1}, respectively[36]. It is estimated that the total cost of nFe_2O_3 was about $700 ha^{-1} (with unit price of $35 kg–1, https://www.alibaba.com/product-detail/SUOYI-Nano-Ferric-oxide-20-30nm_1600374519559.html?spm=a2700.galleryofferlist.normal_offer.d_title.436e4b8bqH7jYM), while the net revenue increase is approximately $160,000 ha^{-1} (with $4.37 kg^{-1} tomato, June 2022, US price; https://fred.stlouisfed.org/series/APU0000712311). In addition, several studies reported a significant increase in plant growth and yield when testing NPs as micronutrients. Owing to the low dosage of micronutrients (that is, ≤50 mg l^{-1} in foliar spray[37]), the risk of NP accumulation in food remains low, as research reported similar metal levels in grain/fruit treated with conventional or nanometal-based fertilizers[26]. It is highly likely that nanofertilizers used as micronutrients can increase net revenue.

We further estimate changes in GHG emissions after nano-N fertilizer is widely adopted. While there are no available data about GHG emissions from nanofertilizer (that we defined in this study using γ) manufacturing, there are several studies demonstrating that simply mixing a small amount of nanomaterials (for example, carbon nanotube[38], 2D graphite carbon NPs[33] and ZnO (ref. [39])) with conventional fertilizers can significantly increase nutrient uptake efficiency and thus reduce the dosage substantially (for example, 30% reduction[33]). Moreover, nanomaterials (such as nanographene oxide[40], nZnO (refs. [41,42]), nFe_2O_3 (ref. [5]) and nAg (ref. [43])) have been proven as effective fertilizers. For example, applying 1 mg nAg kg^{-1} soil (0.3 wt% of N fertilizer dosage) was found to increase grain yield by 42.3% (ref. [43]); 80 mg l^{-1} of nZnO sprayed onto wheat increased yield from 4.38 g per pot (control) and 6.96 g per pot (chemical zinc) to 19.94 g per pot[42]. It is highly likely that optimizing the composition of nanofertilizer can increase γ significantly. Thus, we estimate the GHG emissions from nanofertilizer manufacturing by adding the GHG emissions of conventional fertilizer and those of any nano-additives. In Fig. 4a, it is observed that small GHG emissions of nanomaterials, low weight ratio of nanomaterials added, and high efficiency of the derived nanofertilizers can lead to a significant reduction of the overall GHG emissions during manufacturing. Currently, with a 30% fertilizer dosage reduction (representing a nanofertilizer with γ of 1.4) (ref. [33]), to achieve a goal of GHG emissions reduction from the level of 2019 (the green dashed line in Fig. 4a), the weight ratio of the nano-additive to conventional fertilizer shall be less than 1% and its GHG emissions during manufacturing shall be lower than 200 kg CO_2 kg^{-1}. If mixing 1% of 100 kg CO_2 kg^{-1} nanomaterials into conventional fertilizer reduces fertilizer dosage by 50% or 75% (that is, γ of these nanofertilizer increases to 2 or 4), then the overall GHG emissions during fertilizer (including both nanomaterials and conventional fertilizer) manufacturing can be lowered by 31.2% and 65.6%, respectively, compared with 2019 levels (FAOSTAT, https://www.fao.org/faostat/en/#data/GY).

In terms of the GHG emissions from the applied fertilizer in cropland, seen from Fig. 4b, GHG emissions from conventional N fertilizer usage are predicted to increase to 6.4×10^8, 6.6×10^8 and 6.7×10^8 T (equivalent CO_2 emissions) in 2030, 2040 and 2050, respectively. In contrast, with the use of nanofertilizer GHG emissions may be greatly reduced. For instance, when m (the percentage of conventional fertilizers replaced by nanofertilizer to the overall fertilizer usage) equals 20%, 40% and 50%, GHG emissions in 2050 decrease to 5.5×10^8, 4.3×10^8 and 3.8×10^8 T, respectively ($\gamma = 6$), representing a 17.9%, 35.8% and 43.3% decline, respectively; when γ increases from 3 to 9, if 40% of conventional N fertilizers are replaced by nanofertilizers, then GHG emission will decline from 4.7×10^8 to 4.2×10^8 T in 2050. In sum, a higher efficiency of nanofertilizers could allow for reduced usage, which would lead to reduced GHG emissions.

Case for nanopesticides

According to FAOSTAT (https://www.fao.org/faostat/en/#data/RP), in 2019 the global pesticides use in agricultural practices was about 4.17 million tonnes, which includes 2.22 million tonnes of herbicides, 0.97 million tonnes of fungicides and bactericides, and 0.70 million tonnes of insecticides. Given the large consumption of herbicides, their environmental impact could be greatly reduced if nanotechnology could reduce their usage. Among the different nanoformulations, nanoporous materials (for example, SiO_2 and zeolites), nanomicelles (self-assembled amphipathic co-polymers), nanoemulsions (oil-in-water emulsions) and nanocapsules (typically with a polymeric shell) have been explored as potential pesticides carriers[44]. For instance, two studies reported on the successful preparation and delivery of temperature- and/or pH-responsive nanocarriers for agrochemicals into/onto tomato leaves[28,45]. However, so far, little effort has been placed on nanocarrier development for efficient herbicide loading/delivery and in vivo programmed release. Thus the economic feasibility

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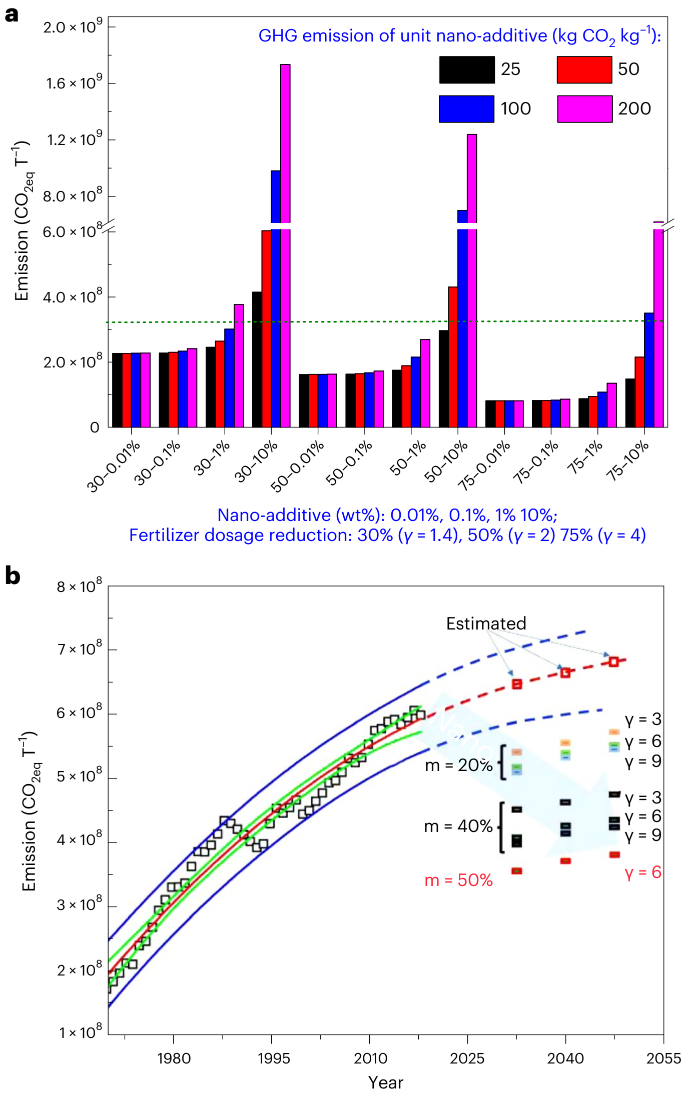

Fig. 4 | GHG emission reduction by using efficient nanofertilizers. **a**, GHG emission during fertilizer manufacturing under different scenarios: 25, 50, 100 and 200 kg CO_2 kg^{-1} are the equivalent GHG emission of different nano-additives during synthesis, such as nZnO, nAg, nCu and nanocellulose (Supplementary Table 1); 30%, 50% and 75% fertilizer dosage reduction represents nanofertilizer with $\gamma = 1.4$, 2 and 4 (the green dashed line represents 2019 GHG emission of conventional N fertilizer during manufacturing). **b**, GHG emission from applied fertilizer in cropland: polynomial fit (red line) was use for data analysis (green line and blue line represent 95% lower/upper confidence interval and lower/upper prediction interval; red dashed line represents predicted GHG emission; □ represents the predicted GHG emission value at that year), and γ and m represent the efficiency of nanofertilizer and the percentage of conventional fertilizers replaced by nanofertilizer. Emission data before 2019 are collected from FAOSTAT (https://www.fao.org/faostat/en/#data/GY).

of replacing traditional herbicides with nano-encapsulated herbicides is largely unknown and needs further investigation once more data are available.

In terms of nanopesticides, we first performed a thorough comparison between conventional pesticides and nanopesticides (in two categories: pesticides in nanocarriers and metal-based nanopesticides) in terms of their efficiency for pathogen/pest inhibition. As demonstrated in Fig. 5a, pesticides in nanocarriers have higher efficiency than their conventional counterparts under a wide range of conditions, with the average efficiency increase from conventional to nanoformulation under the same dosage being about 25.4 ± 11.6%. With regard to the lethal concentration at which 50% of the target pests are killed (LC_{50}) of pesticides, the value of nanopesticides is 50% lower than that of conventional pesticides, with some even an order of magnitude lower (Fig. 5b). This reduction in the mass of active ingredients, although varying over a wide range, contributes to the economic benefit of using nanopesticides. Given the relatively low price of promising nanocarrier materials (https://www.alibaba.com/?spm=a2700.galleryofferlist.scGlobalHomeHeader.8.17be6dc9L79Kg6), such as nanocellulose (\$1–50 kg^{-1}), nanochitosan (\$11–34 kg^{-1}), alginic acid (\$1–6 kg^{-1}) and zein (\$40–50 kg^{-1}), it is very likely that using organic nanocarriers for pesticide delivery will be economically feasible. However, a lower LC_{50} probably means nanopesticide is more toxic to organisms in environment, which needs careful investigation before practical application.

In terms of metal-based nanopesticides, they are classified into Ag, Zn, Cu and other metals (for example, Ti and Mg)-based nanopesticides. We collected LC_{50} values for these nanopesticides (and their conventional counterparts if reported in the literature) to different types of bacteria, fungi and pests. It is widely acknowledged that metal-based NPs can be employed for pest and pathogen control in agricultural practices[46], and they have shown some advantages over their conventional counterparts, such as lower LC_{50} (Fig. 5c). However, as shown in Fig. 5c, the effectiveness of metal-based nanopesticides varies, and it is difficult to find a universal working concentration of a particular type of nanopesticide depending on its LC_{50}. According to literature, the effectiveness has close relationship with size, surface functional group, composition and even crystal structures of the NPs[8,9,46]. it is possible that mixing with a secondary metal[47], biosynthesizing with plant extracts[48] and combining with conventional pesticides[49] can greatly improve the effectiveness of metal-based nanopesticides. With respect to cost, the cost of 378.5 l (100 gallons) of a conventional pesticide solution ranges between \$1 and \$160 (Fig. 5d), with an active ingredient concentration ranging between 0.1 mg l^{-1} and 3.0 mg l^{-1} (based on data from https://www.purduelandscapereport.org/article/fungicide-costs/). For nanopesticides (for example, nAg, $nTiO_2$, nZnO, nCuO and nS_8^0), assuming an effective concentration for pathogen growth inhibition ranges between <10 mg l^{-1} and 1,000 mg l^{-1} (refs. [3,50]), the approximate cost of nAg, $nTiO_2$, nZnO, nCuO and nS_8^0 per a 378.5 l suspension is estimated to be about \$1.14 to \$303, \$0.3 to \$68.22, \$0.038 to \$40, \$0.038 to \$40 and \$1.14 to \$303 (Fig. 5d). As an example calculation, if the price of a nanopesticide is \$100 kg^{-1} and its effective concentration is 100 mg l^{-1}, the calculated cost is approximately \$0.01 l^{-1} (or \$3.79 per 378.5 l) (Fig. 5d, black dashed line), which is far lower than the cost of most conventional pesticides.

In addition, combining NPs with conventional pesticides has been proven to greatly lower the conventional pesticide dosage and improve the efficacy[49,51]. For instance, using nCuO or nZnO as additives to conventional pesticides at an NP concentration of 250 mg l^{-1} can reduce conventional pesticides dosage by 80% (refs. [51,52]). The cost of nCuO or nZnO is approximately \$0.95 to \$10 per 378.5 l suspension, while the reduced conventional pesticides cost ranges from \$0.8 to \$128 per 378.5 l suspension. Therefore, it can be economically feasible to use low-cost NPs, such as nCuO and nZnO, to improve the efficacy of conventional pesticide. Lowering the dosage of NPs, the unit price of NPs and the conventional pesticide concentration (when NPs are present) can further lower the cost of these hybrid pesticides. On the other hand, NPs can be designed to facilitate the degradation of pesticides[52], which can alleviate the environmental impact of conventional pesticides in addition to lowering their dosage.

There have been studies that demonstrate the effectiveness of nanopesticides to endogenous pathogens. While conventional pesticides currently cannot efficiently reach the conducting system of plants, nanopesticides can be properly designed and effectively delivered into the plants to combat these pathogens (Fig. 6). For example, nAg and ZnO/nCuSi can combat *Candidatus liberibacter* and *Xanthomonas citri* subsp. *citri*, respectively, in citrus trees[23,53]. Given the high value of

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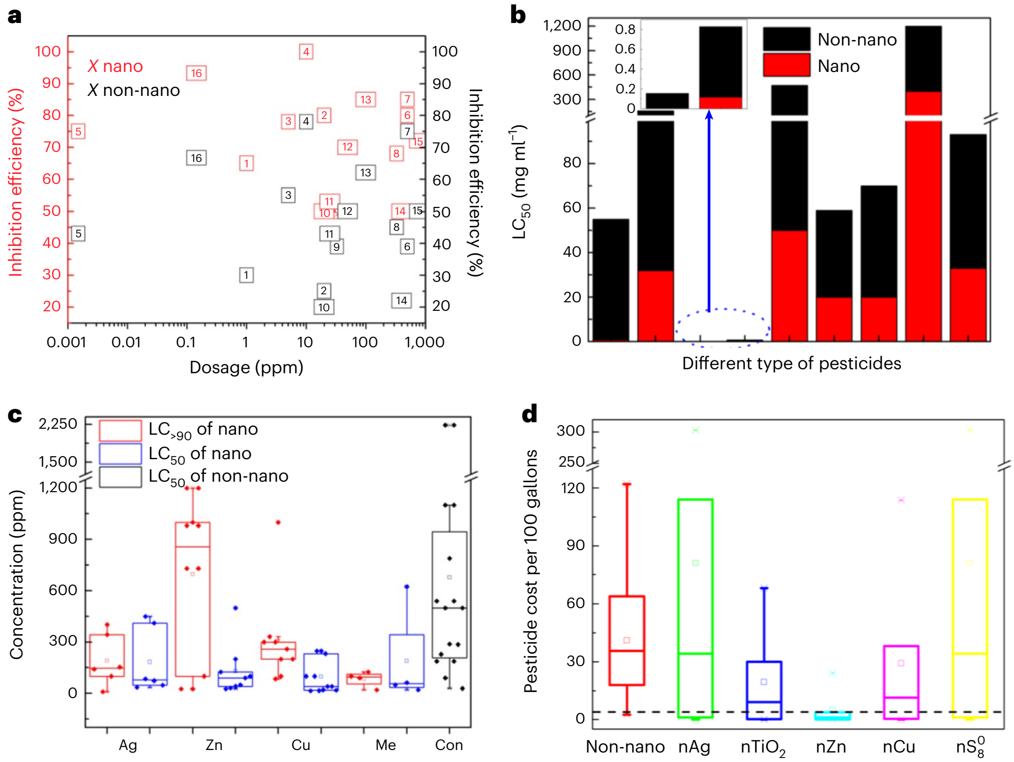

Fig. 5 | Costs and benefits of nanopesticides. a, Inhibition efficacy of nanopesticides (loaded on nanocarriers) and their conventional counterparts on pathogen or pest at the same dosage (data available in Supplementary Table 2). **b**, LC_{50} of nanopesticides (loaded on nanocarriers) and their conventional counterparts (data available in Supplementary Table 2). **c**, LC_{50} and $LC_{>90}$ of metal-based nanopesticides and their counterparts (the box indicates the 25th and 75th percentiles; the stars indicate the maximum and minimum values and the square marker indicates the mean value) (data available in Supplementary Table 3). **d**, Pesticide cost per 378.5 l (100 gallons) working solution (nanopesticide concentration range: 10–1,000 mg l^{-1}; dashed line represents the cost of nanopesticides with unit price as \$100 kg^{-1} and working concentration as 100 ppm) (the box indicates the 25th and 75th percentiles; the stars indicate the maximum and minimum values and the square marker indicates the mean value).

some crops (in Fig. 6), it will be economically viable to use high-value nanoformulations, such as nAg, nS_8^0 and other well-designed nano-complexes, if they are effective in inhibiting growth of pathogens. It is also worth noting that non-food crops account for 5.6% of the total value of crops (\$2.5 trillion) in 2016 (ref. [30]), making it reasonable to incorporate nanopesticide in these non-food crops (such as cut flowers and rubber trees) as well.

Recommendations for future work

On the basis of the above analysis, nanotechnology has the potential to increase the net revenue from agricultural products, especially the high-value crops, and alleviate the environmental impact of conventional fertilizers and pesticides. Given that the efficiency of nanoformulations currently available is relatively low but the price is high, it is possible to use them partially replace conventional counterparts for higher net revenue and better environmental benefits. Further improving the efficiency of nanoformulations is necessary for the wide adoption. Moreover, past research has focused primarily on the effectiveness of nanofertilizers/nanopesticides in crops intended for human consumption (for example, grains and vegetables)[8,22], with studies on animal feed (for example, forages and silage corn), fruit trees and non-food crops still rare. We propose that, in the next phase, research shall focus on the following:

1. **Increasing the efficiency (γ) of benign nano-agents (both fertilizers and pesticides) to increase economic and environmental benefits**. At present, the economic benefit brought by using nanofertilizers/nanopesticides may not be very attractive compared with that of conventional fertilizers/pesticides. For a wide adoption of nano-agents, it is critical to develop benign nano-agents, increase the γ of these nano-agents and reduce the unit cost. The following strategies are recommended: (1) explore green synthesis process via plant extract or functional microbes[54], (2) optimize nanocomposition according to soil conditions, nutrients requirements of plants and climate conditions (that is, droughts, storms and heat), (3) tune NP surface for targeted delivery (that is, to rhizosphere and chloroplast)[55] and (4) minimize the GHG emission of nano-additives and their content in the derived nanoformula. Moreover, it is very likely that nano-agents can be designed to have multiple functions. For instance, nanometals (that is, Fe and Zn) combined with nutrients (that is, N, P and K) and/or conventional pesticides may be able to simultaneously meet the requirements of contamination remediation, nutrient supply, plant immune system improvement and pathogen control. It is also important to realize that there can be long-term environmental implication or carryover benefits of nano-agents, and these aspects deserve more research effort. In addition to lab tests, field tests are needed for estimating the practical economic benefits.
2. **Long-term tracking on NPs in the environment and plants**. Currently, studies on the fate and transport of NPs have been carried out mostly on annual crops, ending after crops were harvested. There is a lack of information on the long-term fate and transport of NPs in environment and plants, especially in cases involving cropland remediation[56] and perennial crops, where the use of nanomaterials may make more economic sense. The physical and chemical properties of NPs evolve after exposure to the environment or after being introduced onto/into plants. The influence of these modified NPs on soil chemistry and the soil

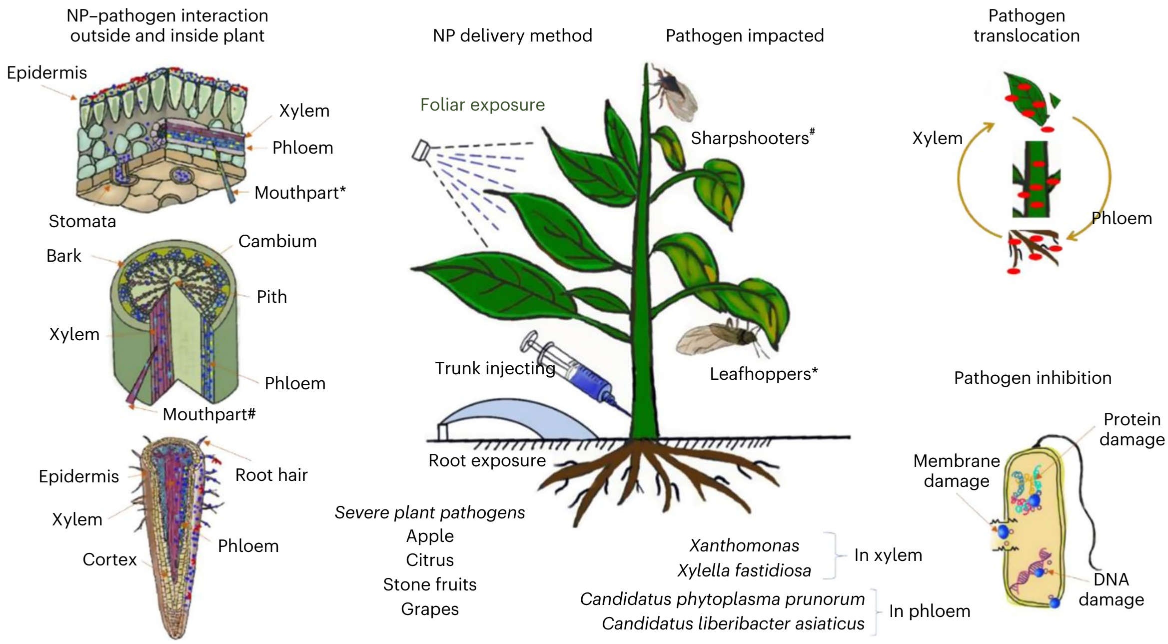

Fig. 6 | Schematic illustration of how nanopesticides potentially combat pathogens in plants (that is, fruit trees infected by xylem- and/or phylem-resident pathogens). Pathogens from soil, irrigation water, and/or vectors (that is, sharpshoots and leafhoppers, feeding on xylem and phloem sap, respectively) can not only colonize on the surface of leaves, shoots and roots but also in the conductive system (xylem and phloem), implying that pathogens are capable to translocate within the whole plant. They will encounter the delivered nanopesticides (via foliar exposure, trunk injection and roots exposure) on different plant tissues and the plant's conductive system. Effective nanopesticides can damage the cell membrane, protein and DNA, thus inhibiting the growth of pathogens. *, mouthpart of leafhoppers; #, mouthpart of sharpshooters.

microbiome, and in particular on nitrifying/denitrifying bacteria (N cycle)[57], needs to be investigated. NP uptake by plants and their fate and translocation within plants needs to be monitored over the long term, as well. In addition, regarding NPs in perennial plants, it remains unknown how these NPs impact photosynthesis, and how NPs impact the properties of plant products (that is, fruit, rubber and timber) in the long term. It will be beneficial if one can manipulate the translocation of NPs in plants, for example, to block NP entry into fruit, and sequester NPs in a particular plant tissue to achieve specific goals.

3. **Developing effective NP delivery methods**. Minimizing the dosage of nanomaterials is critical to limit their cost and environmental release, thus demonstrating the true benefit of nanofertilizers and nanopesticides. Therefore, it is important to develop effective methods for NP delivery in the field, since the current methods developed for dosing conventional fertilizers/pesticides, such as foliar spraying and soil drenching, result in inefficient NP uptake, which can increase the risk of NP leaching into the environment. In terms of trunk injecting and petiole/branch feeding, while they can effectively deliver NPs into larger woody plants (the cost of application is still not available), it remains unclear how to carry out similar injecting or feeding for smaller crops. In addition, the cost of delivery techniques for nanoformulations also needs to be evaluated for practical application.
4. **Developing regulations for nanomaterial use in line with their potential risk for human health**. As there are concerns about the impact of NPs on the ecosystem, the bioaccumulation of NPs through the food chain and the impact of NP-containing foods on human health, besides developing benign NPs, it is necessary to classify different agricultural practices into different categories according to the extent of risk caused by NP use. For instance, NP use in crops planted for energy or materials could be classified into a lowest-concern group, while crops treated with nanomaterials and used for animal feed could be classified into a mid-concern group. For the lowest-concern group, incentives instead of restrictions could be adopted since nanotechnology can lower the environmental cost of conventional fertilizers/pesticides and increase crop revenue. In terms of the mid-concern group, regulatory measures could be designed to encourage farmers to make the best use of nanofertilizers/nanopesticides while minimizing the risk of nanomaterial exposure to human health. For the application of nanomaterials in food crops, it is important to realize there are also major differences between herbaceous and woody plants in terms of the effective dosage, delivery methods, fate and transport of NPs in the plants, and residual NP content in grains and/or (intergenerational) fruit. Therefore, guidelines for nanomaterial application (that is, dosage, dosing time, harvest time and maximum NP content in grain or fruits) in food crops should be crop specific and/or should depend on the residual level of NPs in grains or fruit post-NP application. This is in line with the Approach to Regulation of Nanotechnology Products of the US Food and Drug Administration (FDA): the Agency assess each product on its own merits and does not make broad and general assumption about the safety of products related to nanotechnology (https://www.fda.gov/science-research/nanotechnology-programs-fda/nanotechnology-fact-sheet). In addition, the FDA encourages industry to carry out individual consultation with the Agency to facilitate a mutual understanding about the scientific and regulatory issues related to the agricultural products grown with nanotechnology.

Methods

This study complies with all relevant ethical regulations from each university involved. The cost of nanofertilizers as micronutrients per hectare was estimated through multiplying the total dosage per hectare by the unit price. In terms of macronutrients, while economic benefits can be qualitatively estimated by comparing revenue increase brought by using nanofertilizers with the cost of nanofertilizers, it is of great importance to quantify both economic and environmental benefits for fully embracing nanotechnology in agricultural practices. We use maize and N fertilizer as an example. First, we modify the traditional logistic fertilizer-yield function developed by Reck and Overman[58] as follows (equation (1)),

$$Y = A/\left(1 + e^{\alpha - \beta(X_T + \gamma X_N)}\right) \quad (1)$$

where $Y, A, \alpha, \beta, X_T, X_N$ and γ are actual yield (T ha^{-1}), maximum potential yield (T ha^{-1}), intercept parameter, response coefficient (ha kg^{-1}), traditional N fertilizer dosage (kg N ha^{-1}), nano-N fertilizer dosage (kg N ha^{-1}) and relative efficiency of the nanofertilizer to traditional one, respectively. In this study, γ represents the ratio of conventional fertilizer dosage to nanofertilizer dosage that is needed to obtain an equal yield, and it is assumed to be 1, 3, 4, 5, 6 and 9; these values are based on the typical dosage of the two types of fertilizer from two data resources (https://inscx.com/shop/ and https://ag.purdue.edu/commercialag/home/resource/2017/03/purdue-crop-cost-return-guide/): nano-N 10 kg ha^{-1} versus urea or anhydrous ammonia 123.8–270.0 kg ha^{-1}; nano-P 5 kg ha^{-1} versus P_2O_5 38.2–64.1 kg ha^{-1}; nano-K 5 kg ha^{-1} versus K_2O 59.6–90 kg ha^{-1}. Values of parameters A (9.51 T ha^{-1}), α (0.77) and β (0.013 ha kg^{-1}) are obtained from a study by Reck and Overman, assuming that nanofertilizers were employed to replace the conventional fertilizers used in the cropland reported in the study[58]. It is noted that the quantitative relationship of yield–dosage (using MATLAB R2020a) may vary among different studies owing to the different soil types and cultivating conditions, but the trend was quite similar[59,60]. While Reck and Overman's model allows us to quantitively analyse the impact of nanofertilizer efficiency on dosage–yield relationship, it has to be noted that the accuracy of this model can be influenced by the types of soil, abundance of soil organics, irrigation mode and some other factors[61].

Second, it is hypothesized that the environmental costs associated with fertilizer use primarily include the cost of nitrate leached (C_{L_N}), ammonia volatilization (C_{Am}) and the release of gaseous NO (C_{NO}) and N_2O (C_{N_2O}) (N_2 from denitrification is not incorporated here);[62] we propose to use equations (2–5) to estimate these costs on the basis of the findings from previous studies:[62,63]

$$C_{L_N,X_T} = a \times L_N \quad (2)$$

$$C_{Am,X_T} = b \times R_1 \times [X_T(1 - \mathrm{NUE}) - L_N] \quad (3)$$

$$C_{NO,X_T} = c \times R_2 \times [X_T(1 - \mathrm{NUE}) - L_N] \quad (4)$$

$$C_{N_2O,X_T} = d \times R_3 \times [X_T(1 - \mathrm{NUE}) - L_N] \quad (5)$$

in which a, b, c and d are the environmental cost of leached nitrate (\$2.44 kg^{-1} N), ammonia volatilization (\$11.3 kg^{-1} N), NO (\$29.12 kg^{-1} N) and N_2O release (\$16.18 kg^{-1} N); R_1, R_2 and R_3 are the proportion of ammonia (0.48), NO (0.09) and N_2O (0.09) to the overall mass of N from fertilizer (excluding N utilized by plants and N leached) (notably, N_2 accounts for 34% of the rest of N); NUE is the N utilization efficiency, which heavily depends on irrigation models. Assuming an efficient irrigation system, we use a relatively high NUE value for conventional fertilizer in our model to avoid overestimating the environmental benefits brought by replacing conventional fertilizers with nanofertilizers: 0.67, $X_T \le 50$; 0.62, $50 < X_T \le 100$; 0.57, $100 < X_T \le 150$; 0.54, $150 < X_T \le 200$; 0.52, $200 < X_T \le 250$; 0.5, $250 < X_T \le 300$ (ref. [1]). L_N, leached nitrate (kg N ha^{-1}), can be calculated by the following equation[64],

$$L_N = 68e^{[0.71\times(\frac{X_T}{X_R} - 1)]} - 33.43 \quad (6)$$

in which X_R is the recommended dosage for maize (180 kg N ha^{-1}). In terms of the environmental cost of nanofertilizers, it is assumed that nitrate leaching, ammonia volatilization and the release of NO and N_2O can be reduced by 50%, 10% and 20%, respectively, on the basis of previous findings about NUE improvement strategies[33,34,42,62,65,66]. Notably, nitrate leaching, ammonia volatilization and the release of gaseous NO and N_2O are closely related to NUE[66]. The higher NUE is, the less fertilizer remains in the environment and thus, the fertilizer has a lower environmental impact. This implies that environmental benefits brought by nanofertilizers vary with the degree of NUE improvement.

To simplify the calculation, it is further hypothesized that revenue primarily varies with yield, fertilizer cost and environmental cost. Other expenses, such as pesticides, labour and transportation remain the same between the two scenarios (that is, with and without nanofertilizers), although it is possible that labour expenses may increase owing to the additional training needed for nanomaterial handling. In contrast, transportation expenses may decline owing to the significant reduction in fertilizer mass. Therefore, net revenue (R, \$ ha^{-1}) after adopting nanofertilizers can be expressed by equation (7):

$$\begin{aligned} R = {} & Y_{(X_T,X_N)} \times P - X_T \times p_T - X_N \times p_N - C_{L_N,X_T} - C_{Am,X_T} - C_{NO,X_T} \\ & - C_{N_2O,X_T} - 0.5C_{L_N,X_N} - 0.9C_{Am,X_N} \\ & - 0.8C_{NO,X_N} - 0.8C_{N_2O,X_N} \end{aligned} \quad (7)$$

where P is the price of corn (\$149.0 t^{T-1}, low-end commodity US price, from 2014 to 2020, https://www.indexmundi.com/commodities/?commodity=corn), p_T is the price of traditional fertilizer (\$1.7 kg^{-1}) and p_N is the price of nanofertilizer (\$10 kg^{-1}, https://inscx.com/shop/newshop/). The constants, 0.5, 0.9 and 0.8, are derived from the assumption forementioned that nanofertilizers have lower environmental cost than conventional fertilizer. Notably, the net revenue largely depends on the price of the crop, conventional and nanofertilizers, the efficiency of the nanofertilizer, and the GHG reduction brought by nanofertilizers. While this is a preliminary evaluation (based on US price of crops, fertilizers and pesticides), it is applicable for evaluating the cost–benefit of nanofertilizers to different types of crops under different scenarios. However, owing to a lack of data, the potential environmental impact of nanomaterials is not considered in this model (in the case of large consumption of fertilizers and pesticides, safe and green nanomaterials are highly recommended).

To explore the impact of nanofertilizers use on reducing GHG emissions, we estimated the possible emission change of GHGs during manufacturing and field application. Here, to simplify the estimation of GHG emission during manufacturing, we assume nanofertilizer could be used as a hybrid with conventional fertilizer of nanomaterials, with wt% of 0.01%, 0.1%, 1% and 10%. GHG emission from nanofertilizer during manufacturing ($E_{GHG,pro}$) can be expressed by equation (8),

$$E_{GHG,pro} = \mu_{con} \times \varphi \times (1 - \tau) + \varphi \times (1 - \tau) \times \omega \times \mu_{nano} \quad (8)$$

where μ_{con} and μ_{nano} are the GHG emission of conventional fertilizer ($\mu_{con} = 3$, as urea) and different types of nanomaterial during manufacturing ($\mu_{nano} = 25, 50, 100, 200$) (data of typical nanomaterials are available in Supplementary Table 1), φ is N fertilizer usage in 2019 (1.08×10^8 metric tonnes), τ and ω are percentage of fertilizer usage reduction (τ = 30%, 50%, 75%, representing $\gamma = 1.4, 2, 4$) and weight percentage of nanomaterials to conventional fertilizer.

In terms of GHG emission from field application of N fertilizer, N_2O released after its application has a global warming potential 265–298 times greater than CO_2 on a 100 year timescale. To simplify the calculation, the GHG emission ($E_{GHG,post}$) is assumed to include direct (N_2O_{Direct}) and indirect ($N_2O_{Leaching}$) emissions of N_2O resulting from fertilizer usage, which can be expressed by equations (9–11) (refs. [33,62,64]),

$$E_{GHC,post} = 265 \times (N_2O_{Direct} + N_2O_{Leaching}) \quad (9)$$

$$N_2O_{Direct} = F_{SN} \times EF_1 \quad (10)$$

$$N_2O_{Leaching} = F_{SN} \times Fract_{Leach} \times EF_2 \quad (11)$$

$$F_{SN,nano} = F_{SN,con}/\gamma \quad (12)$$

where F_{SN}, EF_1, $Fract_{Leach}$ and EF_2 are the annual amounts of synthetic conventional N fertilizer applied to soils (kg N per year), the emission factor for N_2O emissions from N (EF_1 0.01), the fraction of N losses by leaching/runoff to total applied N fertilizer ($Fract_{Leach}$ 0.3), and the emission factor for N_2O emissions from N leaching and runoff (EF_2 0.0075), respectively. Owing to the high efficacy of nanofertilizer, F_{SN} of nanofertilizer can be approximately calculated by equation (12). The reduced dosage decreases both the direct and indirect N_2O release. The total GHG emissions consist of the emissions from conventional fertilizer ($E_{GHG,post,con}$) and emissions from nanofertilizer ($E_{GHG,post,nano}$), and can be estimated by equation (13).

$$\begin{aligned} &E_{GHG,post,total} = E_{GHG,post,con} + E_{GHG,post,nano} = (1-m)\,E_{GHG,post,con,total} + \\ &E_{GHG,post,nano} \approx 265 \times F_{SN,con,total} \times \Big[(1-m) \times (EF_{1,con} + Fract_{Leach,con} \times EF_{2,con}) \\ &\quad + \frac{0.8 \times m}{\gamma}\,(EF_{1,con} + Fract_{Leach,con} \times EF_{2,con})\Big] \\ &\quad = (1-m)\,E_{GHG,post,con,total} + \frac{0.8 \times m}{\gamma} E_{GHG,post,con,total} \end{aligned} \quad (13)$$

in which m is the assumed ratio that conventional fertilizer replaced by nanofertilizer to the total expected conventional fertilizer usage ($E_{GHG,post,con,total}$), and the constant 0.8 is obtained from the assumption that nanofertilizer reduces N_2O release by 20% (refs. [33,65]). $E_{GHG,post,con,total}$ is estimated from historical data fitted with a parabolic model.

Last but not least, to qualitatively estimate the cost of nanopesticides, we assume that an effective concentration (M) for pathogen growth inhibition ranges between <10 ppm and 1,000 ppm (refs. [3,50]). The price (p_N) of nAg, $nTiO_2$, nZnO, nCuO and nS_8^0 was found to range between \$300 and \$800, \$80 and \$180, \$10 and \$100, <\$10 and \$100, and \$300 and \$800 kg^{-1}, respectively (depending on particle size and purity). Therefore, the maximum (T_{max}) and minimum (T_{min}) cost of nAg, $nTiO_2$, nZnO, nCu and nS_8^0 per a 378.5 l (100 gallons) suspension are calculated via equations (14) and (15):

$$T_{max} = \frac{(378.5 \times M_{max} \times p_{N,max})}{1000,000} \quad (14)$$

$$T_{min} = \frac{(378.5 \times M_{min} \times p_{N,min})}{1000,000} \quad (15)$$

Reporting summary

Further information on research design is available in the Nature Portfolio Reporting Summary linked to this article.

Data availability

The authors declare that the data (including MATLAB analysis) supporting the findings of this study are available as Excel spreadsheets alongside the manuscript and its Supplementary Information (Supplementary Tables 1–3) and FAO website (https://www.fao.org/faostat/en/#data). Source data are provided with this paper.

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Author contributions
Y.S., A.A.K. and D.J. were responsible for conceptualization, methodology, data collecting and analysis, and writing (original and revised draft). Y.S., P.R., C.R. and D.J. were responsible for project administration and supervision. X.Z., H.M., T.X., H.L., J.E.M. and Y.Z. were responsible for data collecting and analysis, and writing (original draft) and editing (revised draft).

Competing interests
The authors declare no competing interest.

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Data collection	No software was used
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Study description	This study analyzed the cost-benefit of nano fertilizer and nano pesticides
Research sample	Global crop production since 1960 from FAOSTAT; corn yield and fertilizer dosage from literature; cost and benefit of using different types of fertilizers; GHG emission from 1970 from FAOSTAT; efficacy of nano pesticides from literatures; market price of nanomaterials;
Sampling strategy	MATLAB was used to analyze the data from both yield-dosage and cost-benefit model. Data collected from FAOSTAT were analyzed first and surely captured the trend.
Data collection	From FAOSATA
Timing and spatial scale	1970 to 2019, data from FAOSTAT
Data exclusions	No data was excluded
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