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Field efficacy of urease inhibitors for mitigation of ammonia emissions in agricultural field settings: a systematic review

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Globally, ammonia (NH₃) is one of the key air pollutants and reducing NH₃ emissions and the associated indirect emission of the greenhouse gas nitrous oxide remains challenging for the agricultural sector. During the past three decades, a number of urease inhibitors have been placed on the market with the goal of reducing NH₃ loss from urea containing fertilisers. N-(n-butyl) thiophosphoric triamide (NBPT), N-(2-nitrophenyl) phosphoric triamide (2-NPT), a 3:1 ratio of NBPT + N-(n-propyl) thiophosphoric triamide (NPPT) and the maleic and itaconic acid co-polymer (MIP) are registered urease inhibitors under the European Commission Fertilising Products Regulation (FPR). However, the availability of several inhibitor options has raised questions from farmers, policymakers and emissions inventory compiling authorities regarding the field efficacy of the different options available for reducing NH₃ loss. Despite many disparate NH₃ field studies existing for NBPT, 2-NPT, NBPT + NPPT and MIP there is presently no review that brings these results together, a significant and important knowledge gap. This review addresses the gap by summarising the published field trial literature on NH₃ volatilisation mitigation offered by NBPT, 2-NPT, NBPT + NPPT and MIP. Our review identified 48 peer reviewed studies where NH₃ loss mitigation was measured in a field setting, giving 256 replicated comparisons. The synthesised literature results revealed that NBPT + NPPT reduced NH₃ loss by 75% (95% CI = 58–82% n = 32), 2-NPT reduced NH₃ loss by 70% (95% CI = 63–76% n = 19) and NBPT reduced NH₃ loss by 61% (95% CI = 57–64% n = 165), giving on average a 69% reduction by these three urease inhibitors. In contrast, MIP increased NH₃ loss by 0.3% on average (95% CI = –8–9% n = 40). The results presented in this review broaden the understanding of urease inhibitor efficacy in field conditions and demonstrate that not all products behave the same in terms of field NH₃ reduction efficacy. This review is important for farmers, policymakers, emission inventory compilers and other stakeholders.

KEYWORDS

ammonia volatilisation, urease inhibitors, mitigation, nitrogen, urea

1 Introduction

The growing world population has increased food demand, resulting in increased use of organic and inorganic fertilisers to ensure sufficient crop productivity (Gojon et al., 2023; Guo et al., 2023). For example, it is estimated that mineral nitrogen (N) fertiliser supports approximately 46% of global food/feed production (Oita et al., 2016) and global N demand is expected to increase by 5% between 2021 and 2027 (Statista, 2024), such increases would drive further breaches of the safe planetary boundaries for N use set out by Schulte-Uebbing et al. (2022) and Campbell et al. (2017). Strategies to make better use of the N currently in circulation are urgently needed to stem the need for increases in N usage. A major challenge associated with N fertiliser is that on average less than 50% of applied fertiliser N is recovered by plant systems (Tilman et al., 2011) and less by animal systems (5%–30%) (Oenema et al., 2005). Fertiliser N usage is associated with ammonia (NH₃) volatilization, denitrification loss including emission of the potent greenhouse gas nitrous oxide (N₂O) along with nitrate (NO₃⁻) leaching to waterbodies (Scheer et al., 2023) as illustrated in Figure 1. Pan et al. (2016) estimated that at global scale, an average of 18% applied urea N is lost through NH₃ volatilisation. However, losses ranged greatly with between 0.9% and 64% loss being reported (Pan et al., 2016). In 2021, global urea N fertiliser usage was 53.8 million tonnes N (IFA, 2024) as outlined in Table 1. Based on the NH₃ loss value of 18% (Pan et al., 2016) in 2021 approximately 9.7 million tonnes of N was lost through NH₃ volatilisation from urea fertiliser usage globally (Table 1). If this N was retained through NH₃ loss mitigation the projected increases in global N demand could be provided for without increasing N usage. Hence, implementation of NH₃ loss mitigation strategies in farming systems is crucial to stem increases in N fertilisers' usage further beyond the safe planetary boundaries set out by Schulte-Uebbing et al. (2022) and Campbell et al. (2017).

1.1 Effects of NH₃ volatilisation

Ammonia emissions pose a threat to human health worldwide. For example, in Europe and the United States, NH₃ emissions from agriculture contribute to 50% and 30%, respectively of all PM_{2.5} (Erismann and Schaap, 2004). Literature evidence has shown that exposure to PM_{2.5} can cause serious health problems such as lung cancer, chronic obstructive pulmonary disease (COPD) and in some cases PM_{2.5} is associated with asthma and premature mortality (Burnett et al., 2014; Lim et al., 2012). Holst et al. (2018), investigated the association of atmospheric NH₃, particulate NH₄⁺ and the total concentration of PM_{2.5} with incidences of asthma in Danish preschool children ($n = 335,629$) during the period 2006–2012. The authors reported that exposure to high concentrations of NH₃ and its components such as PM_{2.5} may increase the risk for the onset of asthma in preschool children. Furthermore, Lelieveld et al. (2015) estimated that the global PM_{2.5} related mortality in 2010 was 3.15 million people (95% CI = 1.52–4.60 million people). Given that exposure to NH₃ and PM_{2.5} of which NH₃ is a precursor poses a human health threat therefore, it is important to mitigate NH₃ loss from a human health

perspective. Previous studies have concluded that reducing NH₃ emissions is the most effective control strategy for mitigation of PM_{2.5} and its associated adverse health effects (Poizzer et al., 2017; Tsimpidi et al., 2007).

Ammonia loss has financial implications for farmers. For example, globally we estimate (Table 1) that approximately 9.7 million tonnes of N was lost from urea fertiliser through NH₃ volatilisation, and this equates to about US\$6.8 billion (based on Statistica 2023 urea price of US\$707 dollars per tonne N) in direct financial loss of fertiliser. There is a clear rationale for mitigation of NH₃ volatilisation even purely from an on-farm economic perspective.

Ammonia emitted to the atmosphere reacts with aerosols containing sulphuric and nitric acids to create particulates such as ammonium nitrate, ammonium sulphate, and ammonium chloride (Gong et al., 2013; Wyer et al., 2022). These particulates travel and are deposited over short (4–5 km) or long distances (100–1,000 km) from the source (Asman et al., 1998; Krupa, 2003) as either dry particles (dry deposition at velocity of 14 cm s⁻¹) or wet particles (wet deposition during rainfall events at rate of 0.2 cm s⁻¹) (Krupa, 2003; Phillips et al., 2004; Wen et al., 2020) as illustrated in Figure 1. Both wet and dry N deposition processes have been strongly linked with serious environmental concerns such as accelerating eutrophication of water bodies (Draaijers et al., 1989; Kelleghan et al., 2019). Eutrophication can result in declines in aquatic life thus reducing aquatic biodiversity. Furthermore, deposition of NH₃-N on soils and water bodies can cause acidification, which has detrimental effects on the availability of plant nutrient essential elements such as phosphorus, calcium, potassium, and magnesium (Pearson and Stewart, 1993), particularly in low N and sensitive ecosystems including those not under agricultural management. Ammonia volatilisation is regulated by EU laws. Member states must report NH₃ emissions under the National Reduction Commitments Directive and monitor NH₃ concentrations in sensitive areas under, the Habitats Directive (92/43/EEC) (Habitat Council Directive, 1992). The magnitude of reported NH₃ effects on the environment indicates that there is an urgent need for research to find ways to mitigate NH₃ losses from fertiliser use.

While NH₃ volatilization is an international problem, in the European Union (EU) member states have committed to reduce NH₃ losses under the National Emissions Reduction Commitments Directive (2016/2284/EU). Therefore, to meet commitments, NH₃ mitigation practices are urgently needed to reduce NH₃ volatilization in agricultural systems to reduce the economic, environmental, and human health impacts of NH₃ loss.

1.2 Urease inhibitors

To improve the N use efficiency of synthetic mineral fertilisers and to reduce NH₃ volatilisation, several mitigation strategies have been studied and implemented worldwide. The use of specific urease inhibitors have been reported to efficiently minimise NH₃ volatilisation by slowing down urea hydrolysis (Kim et al., 2012; Sha et al., 2023; Watson et al., 1990). Several different inhibitors are commercially available globally. The most widely researched urease inhibitors are phosphorodiamide and phosphorotriamide

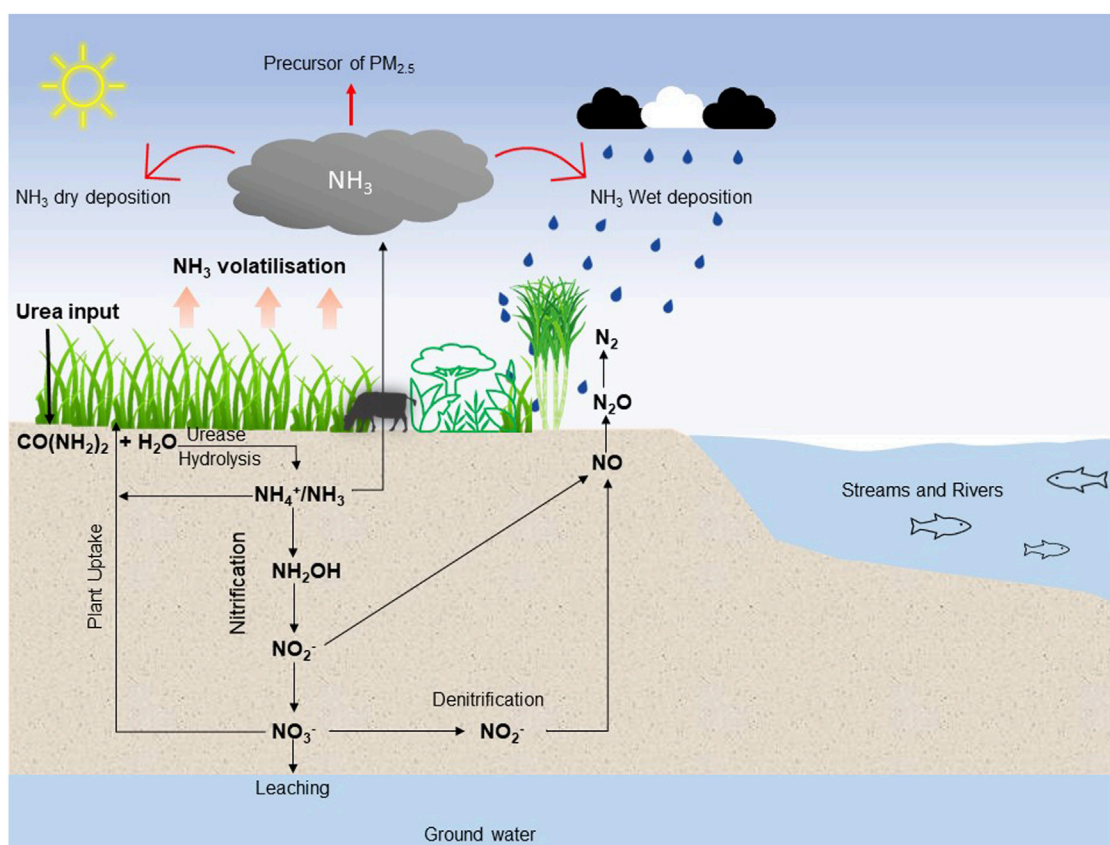


FIGURE 1
Summary only of conversion of applied N fertiliser to mineral N and the N loss pathways.

derivatives (Singh et al., 2023). These include N-(n-butyl) thiophosphoric triamide (NBPT), N-(2-nitrophenyl) phosphoric triamide (2-NPT), and N-(n-propyl) thiophosphoric triamide (NPPT) (Modolo et al., 2018; Song et al., 2022). These phosphoramidate inhibitors, NBPT, 2-NPT and a 3:1 ratio of NBPT + NPPT have been shown to be effective and practically applicable in agricultural field systems. For example, in a field study conducted in New Zealand by Dawar et al. (2011), the authors demonstrated that urea coated with NBPT at 0.1% (w/w) of urea N reduced NH_3 volatilisation loss by 67% on average compared to standard urea in a spring application to a perennial ryegrass (*Lolium perenne* L.) and white clover (*Trifolium repens* L.) sward. Forrestal et al. (2016) reported that application of urea coated with urease inhibitor NBPT (0.066% (w/w) at two grassland experimental sites in Ireland decreased NH_3 volatilisation by 79% on average across the two sites. Similarly, Krol et al. (2020) reported that NBPT and NBPT + NPPT reduced NH_3 volatilisation by 68% on average relative to standard urea. In a 3 year study in winter-wheat conducted by Ni et al. (2014), urea coated with 2-NPT at 0.07 g N kg^{-1} decreased NH_3 volatilisation by 62, 72, and 65% in 2011, 2012, and 2013, respectively. The inhibitory effect of these phosphoramidate urease inhibitors is linked with these inhibitors being a structural analogue of urea as reported in several studies (Byrne et al., 2020; Font et al., 2008; Kot et al., 2001; Mazzei et al., 2017). In research reports, the use of these urease inhibitors has shown promising results, however their widespread application in farm systems has encountered

challenges. There is limited information in literature that depicts which is the most effective urease inhibitor under various soil and climatic conditions.

1.3 Regulation of urease inhibitors in EU

In Europe, NBPT entered the Fertilising Products Regulation (FPR) of the European Commission (EC) as a urease inhibitor under Regulation EC No 1107/2008 of 7 November 2008, 2-NPT under Regulation No 223/2012 of 14 March 2012 and NBPT + NPPT trade name: Limus[®] under Regulation EC No 1257/2014 of 24 November 2014. The regulatory minimum-maximum augmentation of each of these three urease inhibitors based on total N is outlined in Table 2. However, recently the criteria for entry into the EU fertiliser regulations were changed to provide a route via a European Conformity (CE) mark. Briefly, a CE mark is a marking by which the manufacturer indicates that the EU fertilising product is in conformity with set out requirements. The current (2024) CE criteria for a urease inhibitor outline that “a urease inhibitor shall inhibit hydrolytic action on urea ($\text{CH}_4\text{N}_2\text{O}$) by the urease enzyme, primarily targeted to reduce NH_3 volatilisation” this is to be tested by comparing to a control sample where the urease inhibitor has not been added, “an in vitro test containing the urease inhibitor shall show a 20% reduction in the rate of hydrolysis of urea ($\text{CH}_4\text{N}_2\text{O}$) based on an analysis carried out 14 days after application at the 95%

TABLE 1 Global N consumption from urea fertilisers during the 2021 period (IFA, 2024) and potential N losses through NH₃ emissions. Potential NH₃ emissions are calculated based on global meta-analysis by Pan et al. (2016) which reported that an average of 18% of N applied is lost through NH₃ emissions.

Regions	Urea N consumption (million tonnes N)	Potential N loss from urea N through NH ₃ emissions (million tonnes N)
South Asia	20.2	3.64
East Asia	12.7	2.29
Latin America	6.5	1.17
North America	4.3	0.77
Africa	3.0	0.54
West Asia	2.0	0.37
Oceania	1.6	0.29
E. Europe and C. Asia	1.4	0.25
West Europe	1.3	0.24
Central Europe	0.8	0.14
Total world	53.8	9.7

Note: E. Europe = Eastern Europe; C. Asia = Central Asia.

confidence level". Under the CE mark testing NH₃ loss mitigation is not measured (European Commission, 2019). Under the CE mark criteria, the maleic and itaconic acid co-polymer (MIP) was recently granted a CE mark as a urease inhibitor.

However, despite many disparate NH₃ field studies existing for NBPT, 2-NPT, NPPT + NBPT and MIP there is presently no review that compares them, which is an important gap given the pressure to provide NH₃ loss mitigation options to the agriculture sector. Existing reviews focus on NBPT (Silva et al., 2017) and at most one additional inhibitor (e.g., NBPT + NPPT) (Fan et al., 2022; Pan et al., 2016), meaning that 2-NPT and MIP are omitted, a significant gap in literature. Therefore, a broader inter-comparison of all four compounds which focuses on efficacy under field conditions is urgently needed. The focus of the current review on field studies only is a further unique aspect of this review.

2 Materials and methods

2.1 Data search and selection criteria

The present review was conducted to outline the NH₃ loss mitigation effect of adding NBPT, 2-NPT, NBPT + NPPT and MIP to solid urea or urea ammonium nitrate (UAN) liquid. The data synthesised in this study were sourced from peer-reviewed studies collected from the Web of science and Scopus databases. The keywords used during data search were "urease inhibitor/s" OR "NBPT" OR "2-NPT" OR "NBPT + NPPT" OR "Limus" OR "Nutrisphere" OR "MIP" AND "crop systems" AND "pasture systems" AND "ammonia" AND "volatilisation" OR "Volatilization".

TABLE 2 Regulatory minimum and maximum urease inhibitor levels mass of total N as set out by the EU.

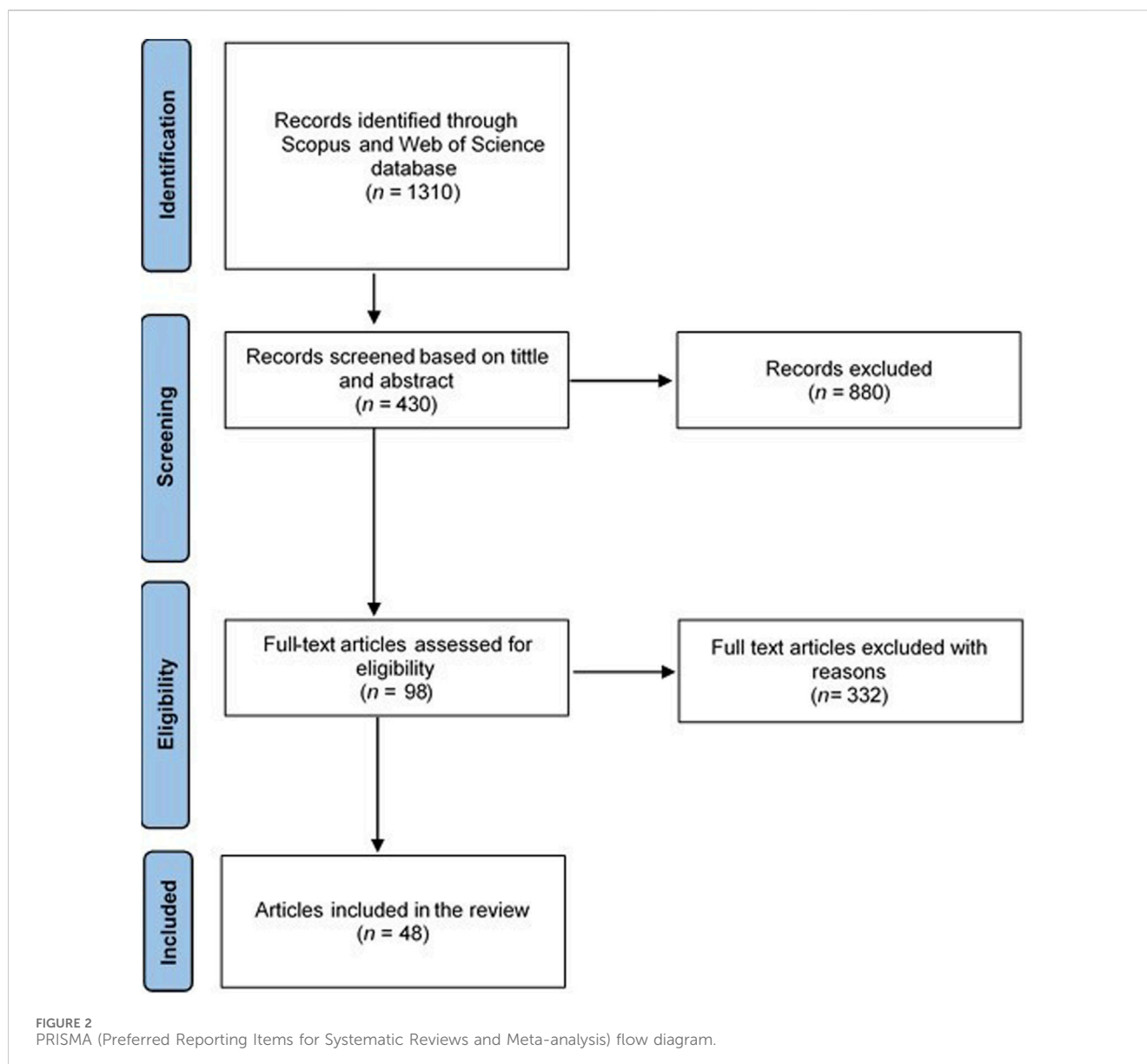
Urease inhibitor	Minimum (%)	Maximum (%)
NBPT	0.09	0.2
2-NPT	0.02	0.3
NBPT + NPPT	0.04	0.15

To evaluate the efficacy of the urease inhibitors, the data was selected based on the following criteria: (a) field study, (b) using either granular urea N or UAN, and (c) the study must include a urea or UAN reference that was not treated with a urease inhibitor. The PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analysis) statement methodology was used to ensure scientific quality (Figure 2). The review considered only peer-reviewed publications. The initial search of literature from Scopus and Web of science generated a total of 1,310 articles. After screening based on title and abstract, a total of 880 articles were excluded leaving 430 articles. Following the review objective which was to compare the efficacy of NBPT, 2-NPT, NBPT + NPPT and MIP for reducing NH₃ volatilisation under field conditions, 332 studies failed to meet the criteria, leaving 98 articles. The full text of these 98 articles were thoroughly evaluated with a total of 50 found not to meet the review criteria. Forty eight (48) articles satisfied the criteria for this review (Figure 2). These 48 peer reviewed papers provided 256 comparisons and were used to evaluate the field efficacy of NBPT, 2-NPT, NBPT + NPPT and MIP. From the individual data sets NBPT had 165 comparisons (from 33 articles), 2-NPT had 19 comparisons (from 2 articles), NBPT + NPPT had 32 comparisons (from 7 articles) and MIP had 40 comparisons (from 6 articles). The data used originated from field testing at experimental sites in 14 countries across Europe, America, Asia and Oceania totalling 79 individual experimental sites. In this review, most of these field studies used the enclosure methods, micrometeorological and wind tunnels methods for NH₃ measurement (Supplementary Table S1). Synthesised data was extracted from published study tables. Data from graphs were extracted using WebPlotDigitizer, <https://automeris.io/WebPlotDigitizer/> as used by Fan et al. (2022) into a database in Microsoft Excel software. All studies summarised in this review are presented in Figures 3A–D.

2.2 Statistical description

In this review, NH₃ mitigation values are presented as a percentage (%) calculated using Equation 1. Following an approach similar to Zheng et al. (2019), in this review a negative value mitigation % in Figures 3, 4 represents decreased emissions from the inhibited fertiliser and a positive percentage indicates increased emissions for the fertiliser with inhibitor relative to the untreated fertiliser.

$$\text{ammonia mitigation (\%)} = \left[\frac{\text{ammonia loss}_{\text{standard fertiliser}} - \text{ammonia loss}_{\text{with inhibitor}}}{\text{ammonia loss}_{\text{standard fertiliser}}} \right] * 100 \quad (1)$$



Mean values of each urease inhibitor were considered significantly different from the untreated control fertiliser when the 95% confidence intervals (95% CI) did not overlap zero. Mean values of each urease inhibitor with 95% CI that overlap each other are considered not significantly different from one another, and *vice versa* as used by Wall et al. (2024) and Fan et al. (2022). All data analysis in this current review was conducted using MiniTab (Version 19. Minitab Inc., United States).

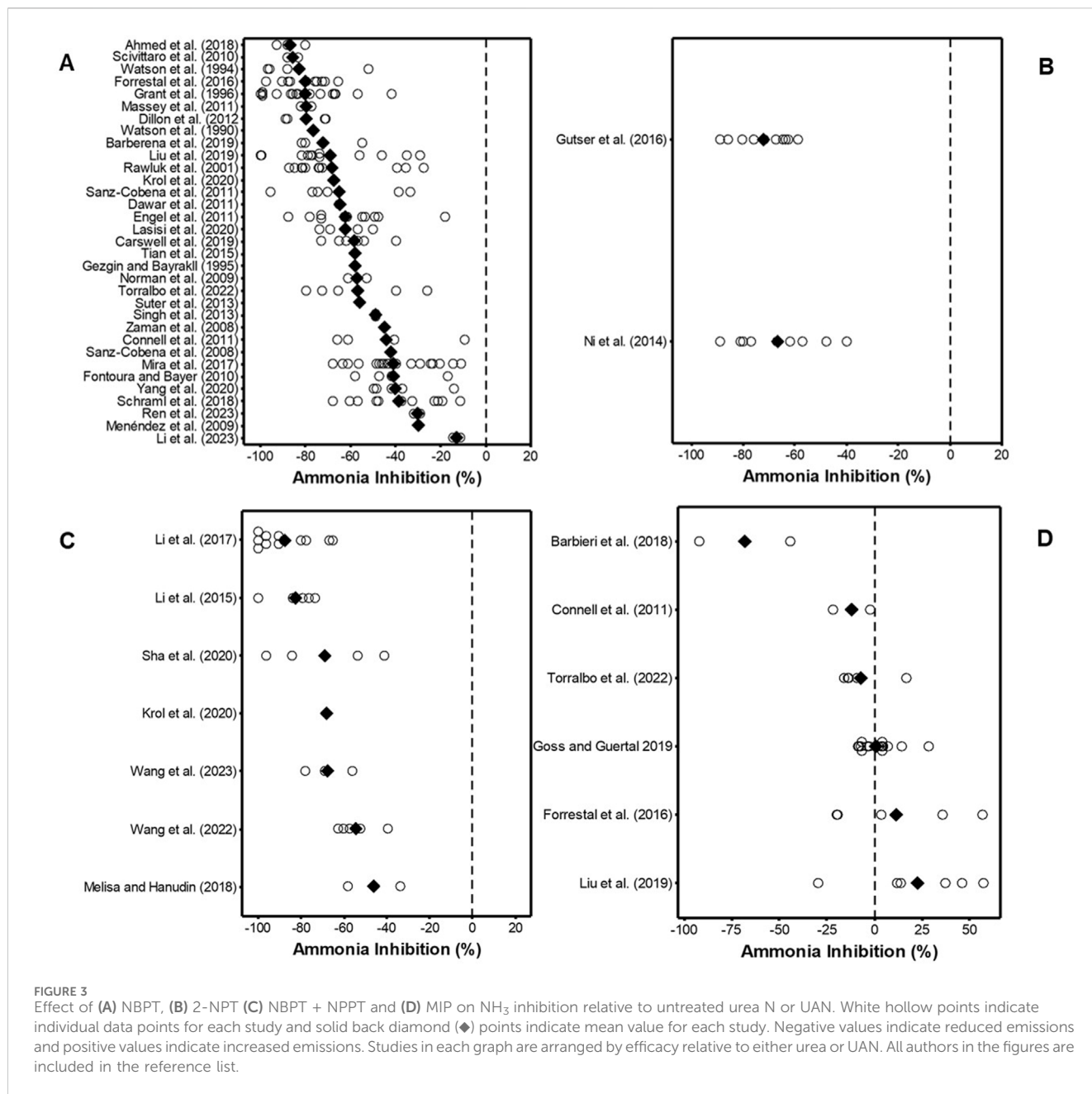
3 Results and discussion

3.1 Mitigation of NH₃ emissions through the use of urease inhibitors

The data displayed in this review (Table 1) shows that urea based N fertilisers are widely used globally for agricultural production thus

measures to protect urea based fertilisers from NH₃ losses have broad applicability globally as well as in the EU.

The data showed that, relative to standard urea or UAN, the phosphoramidate inhibitors NBPT, decreased NH₃ volatilisation by 13%–87% (range of the mean reduction) (Figure 3A), averaging a 61% reduction (95% CI = 57–64%, n = 165) (Figure 4). For 2-NPT, NH₃ emissions were reduced by 67%–72% (range of the mean reduction) (Figure 3B), averaging a 70% reduction (95% CI = 63–76%, n = 19) (Figure 4). The use of NBPT + NPPT with either urea or UAN decreased NH₃ volatilisation by 46%–88% (range of the mean reduction) (Figure 3C), averaging a 75% reduction (95% CI = 68–82%, n = 32) (Figure 4). In contrast, fertiliser N treated with MIP was not significantly different to the untreated fertiliser in the overall analysis, showing data range of –68 to 23 (range of the mean reduction) (Figure 3D), averaging an increase of 0.3% (95% CI = –8–9%, n = 40) in NH₃ loss (Figure 4).



The data synthesised in this review clearly demonstrated that urease inhibitors can potentially reduce NH₃ emissions in field agricultural systems however their efficacy differs. Among the different urease inhibitors, NBPT is the most widely researched urease inhibitor. NBPT has shown successful results ever since its introduction in the mid-1990s up-to-date (Ren et al., 2023; Watson et al., 1990; Zhengping et al., 1991) hence the greater number of available field studies. Results from the current review of global field studies demonstrates that NBPT is effective in decreasing urea fertiliser N losses through NH₃ volatilization in field conditions across a range of soils, crops and environments. Compared to urea or UAN only, NBPT inclusion decreased NH₃ volatilization by an average of 61%, *n* = 165. These mitigation results are lower than the values reported in a meta-analysis by Pan et al. (2016) who found that the use of urea treated with NBPT decreased NH₃

volatilization by 69% on average. The difference between the results may be due to the fact that the current analysis focuses only in field efficacy while Pan et al. (2016) included laboratory incubations. Clough et al. (2007) reported the inclusion of incubation studies has often been associated with greater inhibitor effect than is observed in field studies and highlights the need for a field efficacy focused review where in field effects are needed by farmers, the environment and emissions inventory compilers. The current findings support the report of Clough et al., 2007 which suggested that field studies are associated with differing and reduced efficacy compared with laboratory studies on urease inhibitor efficacy. Thus, while laboratory incubation trials provide a useful proof of concept and mitigation potential, field testing is important to establish efficacy under *in-vivo* conditions.

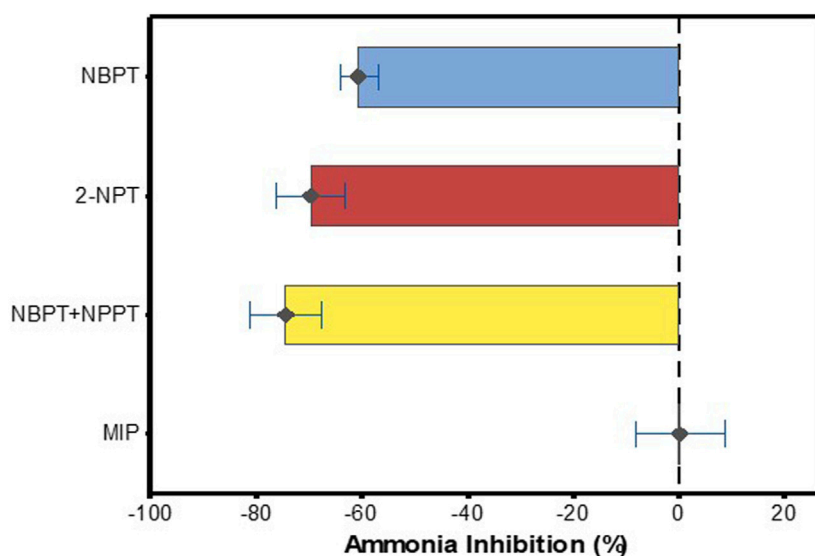


FIGURE 4
Effect of NBPT, 2-NPT, NBPT + NPPT and MIP on NH_3 volatilisation relative to untreated urea N or UAN. Error bars show 95% CIs. Black diamonds (◆) points indicate mean value for each inhibitor from the synthesised data. 95% CIs that overlap with zero indicate no significant difference from the control (urea or UAN without inhibitor) treatment. Negative values indicate reduced emissions and positive values indicate increased emissions.

The reduction in NH_3 loss with the incorporation of NBPT has been shown to improve plant N recovery. For example, Krol et al. (2020) reported that urea plus NBPT significantly increased N recovery in perennial ryegrass (*L. perenne* L.) by 16% (31 kg N ha^{-1}) relative to standard urea. Similarly, Dawar et al. (2011) reported that urea treated with NBPT significantly increased N recovery by 22% compared to standard urea. Furthermore, Hartly et al. (2017) reported that application of urea coated with NBPT increased N uptake by of 9.8 kg N ha^{-1} across three locations over 2 years covering a range of soils and climatic conditions.

This review of the published field trial data on the urease inhibitor 2-NPT, introduced in the market in the 2000s, indicates a mean loss mitigation of 70%, $n = 19$ (Figure 4) compared to untreated fertiliser. Worth noting is that the 2-NPT data was extracted from two published manuscripts. Limited field studies have been conducted with 2-NPT and the lack of more field studies on 2-NPT is associated with more focus on NBPT which was introduced in late 90s. Nevertheless, in these synthesized studies, the use of 2-NPT was shown to be effective. Adhikari et al. (2019) showed that 2-NPT has greater longevity than NBPT. The stability of 2-NPT in soil relative to NBPT has been reported in other studies that have shown similar effects. Domínguez et al. (2008) found that the application of 2-NPT at 0.5% (w/w of N) inhibited urease activity by 65% and 12% after 10 and 30 days, respectively, while NBPT applied at the same rate inhibited urease activity by 40% and 0% after 10 and 30 days, respectively. The use of 2-NPT in conjunction with urea in field studies has consistently shown effective inhibition of NH_3 loss. Furthermore, the use of 2-NPT has given NH_3 loss mitigation from dairy cow urine patches under field conditions. Adhikari et al. (2020) used 2-NPT with $589.7 \text{ kg N ha}^{-1}$ dairy cow urine during late-autumn (New Zealand) in Manawatu fine sandy loam soil (pH 5.5) in a perennial ryegrass (*L. perenne* L.) and white clover (*T. repens* L.) sward. Adhikari et al. (2020) reported that the application of 0.25% of 2-NPT reduced NH_3 loss by 73% when 2-

NPT was applied immediately (0 h) with urine and by 41% when 2-NPT was applied 3 hours after urine application. In the same study, the authors demonstrated that adding urine-N (730 kg N ha^{-1}) 28 days after 0.21% 2-NPT application in summer (New Zealand) led to a 20% reduction in NH_3 loss. Furthermore, Adhikari et al. (2020) reported that the application of urine + 2-NPT increased N recovery by an average of 1.3% (8 kg N ha^{-1}) and 0.6% (4 kg N ha^{-1}) in New Zealand summer and autumn, respectively compared to the urine only treatment across the different application periods studied.

The synthesised field studies data showed that the use of the urease inhibitor NBPT + NPPT decreased NH_3 losses in field studies by an average of 75%, $n = 32$ (Figure 4). The reduction in NH_3 volatilisation induced by the use of NBPT + NPPT has been shown to increase N use efficiency in crops. For example, Wang et al. (2023) demonstrated that the use of urea with NBPT + NPPT at 0.1% (w/w) increased N recovery in a 2 years field (2019–2021) maize-wheat rotation in China by more than 20% compared to standard urea treatment. Krol et al. (2020) reported that the N recovery in perennial ryegrass (*L. perenne* L.) was increased by 8% (16 kg N ha^{-1}) by use of NBPT + NPPT urea relative to standard urea. These findings are further supported by Li et al. (2015) who showed that plant N recovery increased by 10%–16% when urea was treated with NBPT + NPPT.

In this current review, the overall analysis of field trials showed that MIP gave a mean NH_3 emission increase from urea containing fertilisers of 0.3% (95% CI -8 to +9%), $n = 40$. MIP has recently acquired a CE mark as a urease inhibitor in Europe. The proposed mode of action of MIP in reducing NH_3 volatilisation is associated with the maleic-itaconic acid co-polymer binding directly to the active site of the nickel ions found in the urease enzyme (Chien et al., 2014). Mazzei et al. (2018) tested the mode of action of MIP in an *in-vitro* study using purified urease at pH 7.5 and pH 5.0 in a pure environment with no soil or plants present. The study found that urease was not affected by MIP at pH 7.5 but the enzyme was

completely inhibited at pH 5.0 by using MIP at the rate 0.4–2.4 $\mu\text{mol L}^{-1}$. Mazzei et al. (2018) state that “MIPs have no significant inhibitory effect on urease activity at pH 7.5, a condition in which, on the other hand, NBPT inhibits the enzyme”. They reported that NBPT inhibited urease at both pH levels tested. Furthermore, Mazzei et al. (2018) state that their results “Confirms previous reports stating that MIP has no effect on urease activity in urea-fertilized soils in the pH range 5.9–7.3 (Franzen et al., 2011) or 6.5 to 8.1 (Goos, 2013)”. Goos (2018) conducted a study to determine if the findings of Mazzei et al. (2018) could be replicated when soil was included (three soils were used with pH levels of 4.5, 5.2, and 5.7). NBPT was also tested on the same soils. Goos (2018) reported that application of 5 mg kg^{-1} of NBPT inhibited urease activity by an average of 49% across all three soils, compared to 3% and 1% inhibition induced by 5 and 50 mg kg^{-1} of MIP across all three soils. Goos (2018) states that “The observation that MIP inhibits purified urease at a pH of 5.0 could not be repeated with soils with pH values near 5.0”. In the current review in Figure 3D, two points –90% and –44.4% are seen. Both points come from a field study by Barbieri et al. (2018) who reported that application of MIP at 0.25% w/w in a maize field significantly reduced total NH_3 losses and the average 2 year reduction was 65% relative to standard urea. In contrast, Connell et al. (2011) reported that urea treated with MIP did not show significant differences in NH_3 loss relative to standard urea. Furthermore, in a field study conducted by Forrestral et al. (2016) in Ireland, the authors found that application of urea 40 kg N ha^{-1} coated with MIP applied on five separate applications in a moderately drained loam soil did not show a significant reduction in NH_3 loss relative to standard urea. Liu et al. (2019) reported that use of MIP at 0.1% (w/w) in a maize field significantly increased NH_3 emissions by an average of 24.5% relative to standard urea across six experimental sites between 2013 and 2015. In controlled laboratory incubations, the use of MIP has shown some contrasting results. For example, in an incubation study conducted on one soil by Harty et al. (2023) urea coated with MIP (2.1 L Nutrisphere-N[®] tonne^{-1} urea) significantly reduced NH_3 fluxes by 86% relative to the urea only treatment. Harty et al. (2023) conclude that “In controlled conditions, Nutrisphere-N[®] successfully reduced NH_3 emissions compared to urea, and a field assessment of the NH_3 emissions from urea, Nutrisphere-N[®] and other N inhibitors compared to urea is recommended.” Again emphasising the importance of field studies or reviews such as the present review that focus on field studies. In marked contrast to Harty et al. (2023) in a much larger laboratory incubation study using 79 soils representing a wide range of soil properties, Sunderlage and Cook (2018) reported that application of urea + MIP did not significantly ($P = 0.9707$) reduce NH_3 loss across soils. In the same study NBPT + NPPT significantly reduced NH_3 loss. Sunderlage and Cook (2018) concluded that “Although NBPT + NPPT significantly reduced NH_3 -N loss compared with untreated urea, MIP did not and should not be used as protection against volatilization”. Goos and Guertal (2019) reported NH_3 inhibition of 6.8% (not significant) on average using MIP conducted in North Dakota, United States using sandy loam soil, pH = 7.3. The current review of field studies indicates that MIP, on average increased field NH_3 loss by 0.3% (95% CI = –8 to +9%). In contrast, the phosphoramidate inhibitors gave an NH_3 reduction of 61% (95% CI = 57–64%), (NBPT), 70%

(95% CI = 63–76%) (2-NPT) and 75% (95% CI = 68–82%) (NBPT + NPPT) under field conditions.

The use of urease inhibitors such as NBPT, 2-NPT and NBPT + NPPT has shown effectiveness in reducing NH_3 volatilisation. However, previous studies have highlighted that their efficacy is influenced by soil, environmental and management factors. For example, Engel et al. (2015) investigated the effect of soil pH on NBPT degradation, they tested 10 mg NBPT kg^{-1} soil at pH 5.1, 6.1, 7.6 and 8.2. The study reported that the calculated half-life of NBPT was 0.07, 0.59, 2.70 and 3.43 days at soil pH 5.1, 6.1, 7.6 and 8.2, respectively. The authors concluded that degradation of NBPT is affected by soil pH, with faster degradation under the more acidic conditions. Goos (2018) explored the effect of NBPT on urea hydrolysis using three soils on a pH gradient, i.e. 4.5, 5.2 and 5.7 and they found that simultaneous application of urea (2.5 mg of urea per 5 g soil) and 5 mg NBPT kg^{-1} soil inhibited urea hydrolyses by 39, 63 and 75% at soil pH 4.5, 5.2 and 5.7, respectively. Watson et al. (1995) investigated the effectiveness of NBPT following application to 16 grassland soils and reported that the inhibition of NH_3 loss was affected by soil type. The authors found that at 0.28% (w/w) NBPT rate, NH_3 loss inhibition ranged from 54.4% to 99.4% in the different soils. Watson et al. (1995) also reported that the efficacy of NBPT was significantly and positively correlated with soil pH-H₂O ($r = 0.826$, $P < 0.001$).

Soil texture has been shown to also influence the efficacy of urease inhibitors in field studies, showing lower efficacy in fine textured soils than in coarse textured soils (Fan et al., 2022; Gioacchini et al., 2002). This reduced effectiveness of urease inhibitors on fine textured soil has been discussed by Gioacchini et al. (2002), who linked the soil texture effect with the potential strong adsorption of inhibitors to clay fractions in fine textured soil thus reducing their efficacy. Chakraborty et al. (2023) suggested that the high water content in fine textured soil due to their higher water holding capacity can accelerate the degradation of inhibitors in these soils compared with coarse-textured soils.

Furthermore, the inhibitor rate used has been shown to influence the efficacy of urease inhibitors. Watson et al. (1994) reported that field application of urea amended with NBPT at 0.01, 0.05, 0.1, 0.25% and 0.5% (w/w) urea weight basis gave NH_3 loss reductions of 52, 83, 88, 96% and 97%, respectively. Their findings demonstrated that increasing the rate of NBPT increased efficacy. In a later incubation study, Watson et al. (2008) evaluated the effect of NBPT addition rates (0.01, 0.025, 0.05, 0.075% and 0.1% (w/w)) urea weight basis to either coated urea or adding to UAN solutions with four contrasting soil types. The authors found that the average NH_3 reduction over all soils and formulations was 61, 70, 74, 79% and 80% at 0.01, 0.25, 0.05, 0.075% and 0.1%, respectively, again highlighting the importance of inhibitor rate. Indeed, the EU FPR set-outs minimum and maximum inhibitor augmentation percentage by mass of the total N in Europe (Table 2). In Ireland, the application of urea coated with NBPT 0.066% (w/w) was shown to be effective in reducing NH_3 loss by 79% on average across 10 applications at two grassland sites (Forrestral et al., 2016).

More studies of N treated with 2-NPT, NBPT + NPPT and MIP are still needed to better assess the effect of each soil property, environmental conditions and management factors on the effectiveness of these urease inhibitors in field conditions. Based on this review, researchers should ensure that the inhibitor rate, soil

pH and texture are reported when publishing work as this information is not always provided.

4 Conclusion and future prospects

The present review of published field trials found that the addition of the phosphoramidate urease inhibitors NBPT, 2-NPT and NBPT + NPPT to both solid urea and liquid urea containing fertilisers such as UAN reduced NH_3 volatilisation. For these three inhibitors on average the NH_3 reduction was 69%, $n = 216$. However, from the available field studies the effect of MIP on NH_3 volatilisation was not different to zero, giving on average a 0.3% (95% CI -8 to +9%) increase. These results demonstrate that not all products behave the same in terms of field NH_3 reduction efficacy, which is important for farmers, policymakers, emission inventory compilers and other stakeholders. Even-though NBPT, 2-NPT and NBPT + NPPT showed NH_3 loss mitigation results across a range of field studies there is evidence from literature that their efficacy is influenced by soil properties, environmental factors and management practices. The type and rate of inhibitor chosen is one of the key factors affecting efficacy that can be controlled and should be considered carefully. The field trial literature data compiled in this study can be used to inform industry, policy makes, farmers and other stakeholders on the current evidence regarding urease inhibitor efficacy in agricultural field settings. The use of urease inhibitors can help to reduce N loss through NH_3 volatilisation. If the average reduction of 69% was achieved for all urea there is potential to reduce the global NH_3 -N losses from urea alone from 9.7 to 3.0 million tonnes of urea-N. Such savings could be used to offset projected increased demands for total fertiliser N usage globally.

To achieve a better understanding and adoption of the urease inhibitors in agriculture field settings, the following area of research need to be strengthened.

1. The degradation of urease inhibitors during storage is an important factor that will affect their ultimate field efficacy. Therefore, more studies are needed on the degradation characteristics of these urease inhibitors during fertiliser product storage. Some studies have been done with NBPT (Lasisi et al., 2020; Sha et al., 2020) but limited or no previous studies have been published showing degradation rates with 2-NPT, NBPT + NPPT and MIP. A layer of confidence is provided in Europe where a regulatory minimum levels exist which define the inhibitor levels that must be present on the fertiliser at the point of sale. Assurance regarding inhibitor content is important for farmers and highlights the importance of inhibitor degradation studies and regulation in the sector.
2. Field research studies are needed to understand the effect of soil, environmental and management factors on the efficacy of 2-NPT, NBPT + NPPT and MIP as there is more limited published information for these compared to NBPT due to their more recent availability.
3. More research is needed to develop advanced models that can simulate the efficacy of urease inhibitors at global scale based on environmental factors, management practices and soil properties.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary Material, further inquiries can be directed to the corresponding author.

Author contributions

DM: Data curation, Formal Analysis, Methodology, Software, Validation, Writing–original draft, Writing–review and editing. DK: Conceptualization, Funding acquisition, Validation, Writing–original draft, Writing–review and editing. KR: Conceptualization, Funding acquisition, Resources, Validation, Writing–original draft, Writing–review and editing. MD: Conceptualization, Funding acquisition, Investigation, Validation, Writing–original draft, Writing–review and editing. EC: Conceptualization, Funding acquisition, Investigation, Methodology, Writing–original draft, Writing–review and editing. XW: Data curation, Investigation, Validation, Writing–original draft, Writing–review and editing. PF: Conceptualization, Data curation, Funding acquisition, Methodology, Validation, Writing–original draft, Writing–review and editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary Material for this article can be found online at: <https://www.frontiersin.org/articles/10.3389/fenvs.2024.1462098/full#supplementary-material>

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