Plant Nutrition and Fertilizing

Safety, utility and practical use of synthetic Nitrification Inhibitors (SNI)

Statement of the IVA on a study by Frelih-Larsen on biological NIs

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Inhalt

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1. Summary/ Zusammenfassung

Nitrification inhibitors (NI), especially synthetic NI (SNI), are extensively tested and approved technologies for improving the N-efficiency of mineral and organic fertilization. Their use significantly contributes to targeted plant nutrition through fertilizers. They have been proven to reduce nitrate leaching into groundwater and greenhouse gas emissions (GHG) in the form of nitrous oxide. The reduction in losses leads to increased nitrogen use efficiency. While the overall benefits of SNI are not questioned in a recent study by Frelih-Larsen et al. (2022), the ecological safety of SNI is being doubted, and biological NI (BNI) is presented as a supposedly safer alternative with similar benefits. However, due to the authors' limited literature review, there are glaring misjudgements regarding the benefits and risks of BNI compared to SNI. The GHG reduction potential of SNI has been examined and proven through various studies conducted under different field conditions worldwide, accounting for changes in soil, weather conditions, management decisions, and interactions between these factors. On average, a reduction of 44% in nitrous oxide emissions (10-65%, Grados et al., 2022) has been observed. SNI thus possess the highest potential among other agricultural practices to reduce nitrous oxide emissions. Comparable studies are lacking for the use of BNI, with their effects primarily investigated only in laboratory experiments.

Unlike SNI, BNI are only subject to the EU REACH regulation under specific conditions, which requires comprehensive characterization of toxicity and ecotoxicity for chemical products. Furthermore, their approval is either granted at the national level or at the EU level through specific fertilizer regulations. SNI, on the other hand, are regulated as a separate product functional category (PFC 5 A) in the EU Fertilizer Products Regulation. In addition to comprehensive approval requirements, there is ongoing quality and risk monitoring, conducted by national authorities such as the Düngemittelverkehrskontrolle in various countries even after the registration process.

Studies conducted within this framework and additional research confirm the safety of SNI concerning soil organisms (e.g., earthworms), aquatic organisms, as well as other flora, fauna, and human health. One commonly cited negative example involves the detection of minimal residues of SNI in New Zealand milk powder, which was attributed to improper application of pure NI on grassland without the simultaneous use of fertilizers. This practice is no longer common in New Zealand and is practically non-existent in Europe. There is no approval process or comparable studies regarding the safety of BNI as a product and its application at the international, European, or national levels.

Typically, modern SNI are applied at rates ranging from 0.1 to a maximum of 3.2 kg per hectare per year in combination with mineral fertilizers or as an additive to liquid organic fertilizers (e.g., manure). To achieve an equivalent effect in terms of GHG reduction and nitrification inhibition using BNI, an application rate of 1,500 kg per hectare (e.g., of linolenic acid) would be required. Regardless of the practicality and cost of such a measure for farmers (approximately 500 to 15,000 times the application rate compared to SNI), toxicological and ecotoxicological effects are highly likely at such

quantities. Research on the risks associated with BNI is also lacking. Systemic measures such as integrating specific plants to enrich BNI in the soil through root exudates or genetically modifying crops are either impractical for productive and sustainable agriculture or legally inadmissible. In addition to unresolved approval issues, lack of practicality, a lack of evidence of effectiveness, particularly under practical conditions, and the missing proof of toxicological and ecotoxicological safety, there is also the question of the specific targeted benefit of BNI. Statements regarding the course and duration of effects are also absent, as well as studies on degradation and displacement behavior in the soil. As a result, the objectives of using NI are not met, ultimately leading to higher costs for the environment. Therefore, BNI is not suitable for an ecologically safe reduction of GHG emissions in agriculture and, on the other hand, fails to adhere to the principles of good professional practice. Additionally, unlike SNI, their safety has not been proven.

Nitrifikationsinhibitoren (NI), vor allem synthetische NI (SNI), sind eine umfassend geprüfte und zugelassene Technologie zur Verbesserung der Stickstoff-Effizienz mineralischer und organischer Düngung. Ihr Einsatz trägt wesentlich zu einer bedarfsgerechten Pflanzenernährung der Düngemittel bei. Nachweislich werden die Auswaschung des Nitrats ins Grundwasser und von Treibhausgas-Emissionen (THG) in Form von Lachgas signifikant reduziert. Die Verminderung von Verlusten führt zur Erhöhung der Stickstoffnutzungseffizienz.

Während der Nutzen der SNI in einer kürzlich erschienenen Studie von Frelih-Larsen et al. (2022) im Grundsatz nicht bezweifelt wird, wird jedoch die ökologische Sicherheit von SNI hinterfragt. Biologische NI (BNI) werden als vermeintlich unbedenkliche Alternative mit gleichen Vorteilen gegenübergestellt. Durch die eingeschränkte Literaturrecherche der Autorinnen und Autoren ergeben sich jedoch eklatante Fehleinschätzungen bezüglich des Nutzens und des Risikos von BNI im Vergleich zu SNI. Das THG-Reduktionspotenzial von SNI wurde durch verschiedenste Studien in verschiedenen Weltregionen auch unter Feldbedingungen überprüft und nachgewiesen. Veränderungen des Bodens, der Witterungsbedingungen, Bewirtschaftungsentscheidungen sowie Interaktionen dieser Einflussfaktoren wurden in den Studien berücksichtigt. Im Mittel konnte eine Reduktion der Lachgasemissionen um 44 Prozent (10-65 Prozent, Grados et al. 2022) festgestellt werden. SNI besitzen damit auch im Vergleich zu anderen pflanzenbaulichen Maßnahmen das höchste Potenzial zur Verminderung von Lachgasemissionen. Vergleichbare Studien fehlen für den Einsatz von BNI, deren Wirkung überwiegend nur in Laborversuchen untersucht wurde.

Anders als SNI unterliegen BNI nur unter bestimmten Voraussetzungen der EU REACH-Verordnung, die für das Inverkehrbringen von chemischen Produkten u.a. eine umfassende Charakterisierung hinsichtlich Toxizität und Ökotoxizität voraussetzt. Des Weiteren erfolgt die Zulassung entweder national oder auf EU-Ebene über das spezielle Düngemittelrecht. So sind SNI als eigene Produktfunktionskategorie (PFC 5 A) in der EU-Düngeprodukteverordnung geregelt. Neben umfassenden Zulassungsvoraussetzungen erfolgt eine laufende Qualitäts- und Risikoüberwachung, bspw. durch die Düngemittelverkehrskontrolle der Länder, auch nach dem eigentlichen Registrierungsprozess.

In diesem Rahmen durchgeführte und ergänzende Studien bescheinigen SNI die Unbedenklichkeit gegenüber Bodenorganismen (bspw. dem Regenwurm), aquatischen Lebewesen, sowie für die übrige Flora, Fauna und die menschliche Gesundheit. Ein häufig zitiertes Negativbeispiel betrifft den Fund von minimalen Rückständen eines SNI in neuseeländischem Milchpulver. Diese Rückstände konnten auf eine unsachgemäße Anwendung von reinem NI auf Grünland ohne die Applikation mit Düngemitteln zurückgeführt werden. Eine derartige Anwendung von NI wird heute jedoch weder Neuseeland noch in Europa praktiziert. Ein Zulassungsverfahren und vergleichbare Studien zur

Unbedenklichkeit von BNI als Produkt und deren Einsatz existieren dagegen weder auf internationaler oder europäischer noch auf nationaler Ebene.

Üblicherweise werden moderne SNI in Aufwandmengen von 0,1 bis maximal 3,2 kg pro Hektar und Jahr eingesetzt, in Kombination mit Mineraldüngern oder als Zusatz zu flüssigen organischen Düngern (bspw. Gülle). Für einen gleichen Effekt bezüglich THG-Reduktion und Nitrifikationshemmung durch BNI, müsste bspw. eine Aufwandmenge von 1.500 kg pro Hektar (bspw. von Linolensäure) ausgebracht werden. Ungeachtet der Praktikabilität und der Kosten einer solchen Maßnahme (ca. 500 bis 15.000-fache Ausbringmenge im Vergleich zu SNI), sind toxikologische und ökotoxikologische Effekte bei dieser Menge sehr wahrscheinlich. Untersuchungen zu den Risiken gibt es ebenfalls nicht.

Systemische Maßnahmen wie die Integration von entsprechenden Pflanzen, um BNI im Boden durch bspw. Wurzelexudate anzureichern, oder eine gentechnische Veränderung von Kulturpflanzen sind entweder unpraktikabel für einen produktiven und nachhaltigen Ackerbau oder rechtlich unzulässig. Neben ungeklärten Zulassungsfragen, fehlender Praktikabilität und einem fehlenden Beweis der Wirkung, insbesondere unter praktischen Bedingungen sowie dem zu vermissenden Nachweis der toxikologischen und ökotoxikologischen Unbedenklichkeit, stellt sich außerdem die Frage nach dem konkreten zielgerichteten Nutzen von BNI. Weder sind Aussagen zu Wirkungsverlauf und -dauer noch Studien zu Abbau und Verlagerungsverhalten im Boden vorhanden. Die Ziele des Einsatzes von NI werden dadurch verfehlt und letztendlich höhere Kosten für die Umwelt verursacht.

Insgesamt eignen sich BNI nicht für eine ökologisch unbedenkliche Reduktion der THG-Emissionen aus dem Ackerbau und verfehlen andererseits auch die Grundsätze der guten fachlichen Praxis. Zudem ist deren Unbedenklichkeit im Gegensatz zu SNI nicht bewiesen.

2. Abstract

Nitrification inhibitors (NI), especially synthetic NI (SNI), are a well-tested and approved technology for improving N-efficiency in mineral and organic fertilization. Their use also contributes to targeted fertilizer effectiveness and significantly reduces nitrate leaching into groundwater and greenhouse gas emissions (GHG) in the form of nitrous oxide. A recent study by Frelih-Larsen et al. (2022) questions the ecological safety of SNI and presents biological NI (BNI) as a supposedly harmless alternative with similar benefits. However, due to the authors' limited literature review, there are glaring misjudgements regarding the benefits and risks of BNI compared to SNI. The chemical classification of SNI is regulated through the EU-REACH regulation, while their fertilizer approval is based on national and European legislation. They are defined as a separate product functional category (PFC 5 A) in the EU Fertilizer Products Regulation, and relevant products are continuously monitored by fertilizer traffic control.

Extensive studies have demonstrated the efficacy of SNI under various field conditions, as well as its toxicological and ecotoxicological safety. There is no comparable legislation or body of research regarding the effects of biological NI (BNI). Laboratory experiments assessing the impact of BNI often fail to replicate real-world conditions, and the toxicological and ecotoxicological safety of BNI under the high application rates required (e.g., linolenic acid at 1,500 kg/ha) has not been determined.

In comparison to BNI, SNI exhibits significantly higher effectiveness in reducing emissions and promoting sustainable plant nutrition. It follows a proven and secure authorization and control process with demonstrable safety concerning toxicological and ecotoxicological risks. Additionally, it offers high practicality and cost-effectiveness for farmers.

Nitrifikationsinhibitoren (NI), vor allem synthetische NI (SNI), sind eine umfassend geprüfte und zugelassene Technologie zur Verbesserung der Stickstoff-Effizienz von mineralischer und organischer Düngung. Ihr Einsatz trägt zudem zu einer bedarfsgerechten Wirkung der Düngemittel bei und reduziert nachweislich die Auswaschung des Nitrats ins Grundwasser und von Treibhausgas-Emissionen (THG) in Form von Lachgas. Eine kürzlich erschienene Studie von Frelih-Larsen et al. (2022) zweifelt an der ökologischen Sicherheit von SNI und stellt ihnen biologische NI (BNI) als vermeintlich unbedenkliche Alternative mit gleichen Vorteilen gegenüber. Durch die eingeschränkte Literaturrecherche der Autoren ergeben sich jedoch eklatante Fehleinschätzungen bezüglich des Nutzens und des Risikos von BNI im Vergleich zu SNI. Die chemikalienrechtliche Einstufung von SNI erfolgt über die EU-REACH-Verordnung, die düngemittelrechtliche Zulassung auf Basis nationaler und europäischer Gesetzgebung. So sind sie als eigenständige Produktfunktionskategorie (PFC 5 A) in der EU-Düngeprodukteverordnung definiert und entsprechende Produkte werden laufend durch die Düngemittelverkehrskontrolle überwacht.

Umfangreiche Studien haben die Wirkung von SNI unter verschiedenen Bedingungen in Feldversuchen und die toxikologische und ökotoxikologische Unbedenklichkeit nachgewiesen. Eine vergleichbare Gesetzgebung und Studienlage zur Wirkung von biologischen NI (BNI) existiert nicht. Laborversuche zur Wirkung von BNI sind unter praktischen Bedingungen häufig nicht replizierbar und die toxikologische und ökotoxikologische Unbedenklichkeit von BNI unter den hohen notwendigen Aufwandmengen (bspw. von Linolensäure 1.500 kg/ha) wurde nicht ermittelt.

Im Vergleich zu BNI weisen SNI signifikant höhere Wirkungsgrade im Hinblick auf die Emissionsreduktion und eine nachhaltige Pflanzenernährung, ein bewährtes und sicheres Zulassungs- und Kontrollverfahren mit nachweislich hoher Sicherheit hinsichtlich toxikologischer und ökotoxikologischer Risiken, sowie eine hohe Praktikabilität und Wirtschaftlichkeit für die landwirtschaftliche Produktion auf.

3. Statement IVA on Nitrification Inhibitors (NI)

3.1 Introduction

New fertilizer technologies that reduce losses to the environment and thus increase nutrient use efficiency (NUE) of crops can be summarized with the term “Enhanced Efficiency Fertilizers” (EEFs). EEF mainly cover following three technologies:

- Slow-release fertilizers (SRF): Fertilizing product that releases (converts to a plant-available form) its nutrients at a slower rate relative to a “reference soluble” product. This may be accomplished by biological activity and/or by limited solubility and/or by hydrolysis or other recognized chemical or biochemical means.
- Controlled-release fertilizers (CRF): Fertilizing product that releases nutrients at a controlled rate relative to a “reference soluble” product. The controlled rate of nutrient release is achieved by modifying readily available nutrient forms with recognized physical mechanisms such as coatings, occlusions or other similar means.
- Stabilized N fertilizers (SNF): Fertilizing products to which a nitrogen (N) stabilizer (inhibitor) has been added. A N stabilizer is a substance added to regular fertilizers which extends the time the

N component of the fertilizer remains in the soil in urea (urease inhibitor (UI[1])) or ammonium form (nitrification inhibitor (NI[2])).

Both UI and NI can be further separated into biological (BUI, BNI) and synthetic compounds (SUI, SNI). NIs can be added to all urea- and/or ammonium containing fertilizers (including organic N containing fertilizers). Addition of UI is appropriate only for urea containing fertilizers and this is also the case regarding a combination of UI and NI.

Frelih-Larsen et al. (2022) evaluated the mitigation potential of NI as a climate friendly solution for soil management. Based on a very limited literature research and therefore on only a few, selected scientific papers, they summarized that

- NI are problematic both in terms of their climate and their environmental effects
- Especially synthetic NIs
    - are debatable in their efficacy to deliver positive climate impacts
    - can potentially have negative side effects, in particular on soil biodiversity and aquatic organisms,
    - have unclear long-term impacts so that precautionary principles should be applied and their use should be restricted,
- Therefore, biological NIs should be preferred to synthetic NI.

In the following sections we will discuss in detail major findings of Frelih-Larsen et al. (2022). Based on a more profound literature review we provide solid counterproof that NIs and especially SNIs are a well-established, efficient, environmentally beneficial and reliable technology to mitigate climate change, reduce N losses from N fertilization and secure yield and quality of crops.

3.2 Analysis of the assertions

3.2.1 Climate Impacts of NI

Frelih-Larsen et al. (2022) mention uncertain effects of SNI and BNI usage under field conditions. It is generally known that the extent of effects of all agricultural measures (e.g., tillage, crop protection, any application of nutrients, irrigation) applied under open field conditions strongly depends on soil factors (soil type, soil humidity, soil temperature, microflora, etc.) climate factors (temperature, humidity, radiation, rainfall, etc.) and management factors as well as their complex interactions with each other. Therefore, a varying effectiveness of NI can be assumed as the rule when applied to different environments and conditions but does not indicate an inadequate functionality of used NI (e.g., considering nitrous oxide (N2O) mitigation). A number of meta-analyses clearly evidenced that SNI significantly reduce N2O emissions (in a range of 30 to 65%, average values from different meta-analyses) from mineral as well organic N fertilizers and under a substantial number of different environmental conditions (soil, climate and weather as well as management scenarios). This effectiveness is confirmed e.g., by Kanter and Searchinger 2018 (summarizing different meta-

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[1] Urease inhibitor (UI): A substance that inhibits for a certain period of time urease enzymes responsible for the hydrolysis of urea.
UI reduce NH3 losses (which can be up to 64% of applied N, Pan et al. (2016)) from urea on average by 70% (Bittmann et al. 2014). In addition, also indirect and direct N2O emissions can be significantly reduced (e.g., Cowan et al. 2022, Grados et al. 2022)

[2] Nitrification inhibitor (NI): A substance that inhibits for a certain period of time specific soil micro-organisms responsible for the biological oxidation of ammonium (via nitrite) into nitrate.

analysis), Qiao et al. 2015, Ruser and Schulz 2015, Thapa et al. 2016, Xia et al. 2017, Yang et al. 2019, Fan et al. 2022, Lam et al. 2022, Grados et al. 2022, Pan et al. 2023. The last mentioned meta-analysis of Grados et al. (2022) showed a reduction of total N2O emissions by the use of SNI of 44% on average, indicating that the effect on fertilized N is even higher (Dong et al. 2021). By contrast, reliable data for a profound evaluation of BNI-related N2O mitigation (in particular with respect to active agriculture) is barely available and a comprehensive meta-analysis does not even exist. So far, only a few review papers about BNI in general and their N2O mitigation potential in particular are available (e.g., Subbarao et al. 2015, Wang et al. 2021). Most of these investigations were carried out under model conditions. Thus, the implication of Frelih-Larsen et al. (2022) that SNI and BNI can be currently assumed as equivalent with respect to their N2O mitigation efficiency (in particular when considering active agriculture) is misleading and completely ignores the fact that BNI efficiency as well applicability has still to be proven yet.

Therefore, it can be concluded that especially SNI have a well proven specific and environmentally beneficial effect on the reduction of N2O emissions by nitrification (and denitrification) under many different environmental conditions as well as management scenarios.

3.2.2 Effects on soil biodiversity and aquatic organisms

In the European Union (EU) every chemical which is imported into the EU, produced in the EU and/or introduced into the EU market has to be registered under the EU REACh Directive (EU 1907/2006). The requirements for a registration depend on the annual volume (imported, produced or sold) and comprise toxicological and ecotoxicological studies (covering among other things also possible effects on non-target and aquatic organisms) as well as risk assessments. All SNI commercially available in the EU and in Germany have such a REACh registration. In addition to the obligatory REACh registration NIs have to be assessed for conformity (EU legislation) or registered according to national fertilizer regulations. In the new EU Fertilizing Products Regulation (FPR, EU 2019/1009) a minimum REACh data set and a chemical safety report, as well as a thorough risk assessment are required. Also, under, e.g., the German Fertilizer Regulation (Düngemittelverordnung) the regulatory body (BMEL = Federal Ministry of Food and Agriculture supported by its Scientific Advisory Board on Fertiliser Issues) evaluates possible toxicological and ecotoxicological effects of SNI in the registration process based on an extensive number of relevant studies submitted.

In Germany and also other EU member states surveillance authorities (e.g., in Germany: Düngemittelverkehrskontrolle der Länder) are responsible for quality control of marketed fertilizers and fertilizing products. With these authorities, further follow-up and control of products in terms of labelling and chemical composition, also including risk evaluation is given, even after the registration process.

We are not aware of any registrations of BNI under REACh or FPR.
Any demands that toxicological and ecotoxicological studies should not be needed for allegedly natural products, such as BNI are dubious and contradicts the common principle of a proper risk assessment. It is well known that many natural compounds are very toxic, even under a very low dose level.

As contrarily claimed by Frelih-Larsen et al. (2022) SNI are in fact well-studied compounds with a huge scientific backup and a well-known risk classification. They are checked and registered as chemicals and fertilizer additives. In contrast, neither safe applicability nor reliable benefit has yet been demonstrated for the currently known BNI.

Based only on one study (Kösler et al. 2019) Frelih-Larsen et al. (2022) claimed that SNI carry risks for soil health and biodiversity, as they can be ecotoxic for terrestrial and aquatic organisms. However, ecotoxicological effects as occasionally observed in this study are rather related to an inadequate experimental design than caused by the applied SNI. Beside the fact that Kösler et al. (2019) compared two formulated products containing one (in Vizura®) or two SNI compounds (in Piadin®) with an unformulated pure SNI (DCD), the authors tested dose rates of Vizura® as well as of Piadin® which are far beyond recommended and used dose rates of these products (e.g., Pasda and Schmid 2020). Therefore, results of Kösler et al. (2019) concerning ecotoxicity of Vizura® are of no relevance for the recommended application rates of Vizura® used according to good agricultural practice (Pasda and Schmid 2020). Furthermore, they did also not provide evidence of health or environmental risks associated with the use of Piadin® or its active ingredients. Occasionally observed phytotoxic effects are rather more likely to be associated with the formulation agent (liquid N-fertilizer) than with the active ingredients themselves. The inappropriate application of PIADIN® resulted in a tremendous overdosing of the nitrogen supply of the studied plants, which, however, was not taken into account at all.

In addition to the ecotoxicological studies conducted under REACh for 3,4-dimethylpyrazole phosphate (DMPP), SNI in Vizura®; no effects of acute toxicity on earthworm and no effects on the activity of soil microflora), scientists tested the effect of DMPP on different non-target soil organisms. There were no sustainable adverse effects even with very high dose rates (Tindaon et al. 2012, Dong et al. 2013, Maienza et al. 2014, Kong et al. 2016a, 2017, Shi et al. 2016, Zhang et al. 2017).

Also in long-term field experiments, repeated applications of DMPP (Dong et al. 2021, Shi et al. 2017) as well as of DCD (SNI) and NBPT (SUI; Duff et al. 2022, Shi et al. 2017) did not significantly affect the community structure of ammonia oxidizers (Shi et al. 2016). They did not affect the function and the abundance of N cycling communities (Duff et al. 2022) and did not result in long-term shifts in soil bacterial communities (Dong et al. 2021).

The studies carried out within the framework of fertilizer registration show that the active substances in Piadin®, when used correctly, have no effects on earthworm, collembolans, and activity of soil microflora as well as on algae, fish and daphnia. In addition, Tindaon et al. (2012) as well as Růžek et al. (2014) also found that fertilizers containing DCD (and 1,2,4-triazole) do not have a significant negative effect on biological activity in the examined soils. Also, for the development of juvenile brown trout Bruder et al. (2017) couldn’t find any negative impact from DCD application.

We are not aware of any comparable studies with BNI.

In summary, Frelih-Larsen et al. (2022) unjustifiably tried to imply a large gap of knowledge concerning negative impacts of SNI application by just ignoring plenty of studies and registrations procedures, which already clearly evidenced their save and proper application in agricultural practice. Therefore, it can be demonstrably concluded that (in contrast to BNI) currently SNI are well-known and well-studied compounds with regard to their environmental impact.

3.2.3 DCD (SNI) residues

Based on Ray et al. (2021), Frelih-Larsen (2022) mentioned that residues of DCD were detected in milk. Ray et al. (2021) stated that this mmight have been caused by a special practice of DCD application onto pastures in New Zealand: High amounts of DCD have been directly sprayed onto the grass without any N fertilizer. Uptake of DCD by the grazing cows and its excretion with the urine at least was taken into account in this case. As mentioned above, the common and recommended practice worldwide is the application of nitrogen fertilizers treated with NI but not a sole NI application.

Even under worst-case conditions (oral DCD administration to lactating cows), Welten et al. (2016) concluded that the low recovery of DCD in milk is consistent with other compounds used in veterinary medicine and does not pose a significant risk from milk consumption.

3.2.4 Nitrate on human health

Based on Ahmed et al. (2017), Frelih-Larsen et al. (2022) concluded that nitrate (NO3) can threat human health through consumption of drinking water or vegetables with high contents of nitrate. Such an increased uptake of nitrate can lead to various kinds of human cancer, neural tube defects, diabetes and blue baby syndrome. If this assumption were correct, the number of human carcinosis of vegetarians and workers in factories producing nitrate-containing fertilizers (e.g., Zandjani et al. 1994) would be significantly above the average values in society. But this is not the case. Based on their literature review, Leifert and Golden (2000) concluded that "…there is no conclusive epidemiological evidence that dietary nitrates are causally linked to carcinogenesis and methaemoglobinaemia is now recognized to be linked to endogenous nitrite production resulting from gastro-intestinal infection. Conversely, some epidemiological studies show a reduced rate of gastric and intestinal cancer in groups with a high vegetable-based nitrate intake. There is also now a growing body of evidence from physiological studies to suggest a beneficial physiological role of dietary nitrate in gastro-intestinal protection against food borne pathogens, including Helicobacter pylori infection…".

3.3 Practical use and effects

3.3.1 Comparison of amounts of BNI and SNI per hectare

Frelih-Larsen et al. (2022) cited Ma et al. (2021), who reported up to 93.5% reduction in NO3-concentration when applying 1 g of BNI (here linoleic acid) per kg of wet soil. Assuming a soil depth of 10 cm and a specific mass of 1.5 kg per L soil, one hectare soil has a mass of 1.5 mio kg (= 100 m x 100 m x 0,1 x 1000 L/m3 x 1,5 kg per L). So, the BNI amount corresponding to the study of Ma et al. (2021) would be 1500 kg per hectare (= 1.5 mio kg x 0,001 kg BNI). According to the German Fertilizer Regulation modern SNI are allowed to be applied at concentrations ranging from only 0.05% and 1.6% based on the concentration of ammonium-N and/or urea-N contained in the fertilizer. Assuming a common maximum ammonium-N application rate of 200 kg N per hectare and year modern SNIs are applied at annual rates of ca. 100 g to maximal 3.2 kg per hectare only.

It is remarkable that no toxicological and ecotoxicological studies are available for BNI, although they would have to be used in immensely high quantities per hectare compared to SNI or plant protection products. The necessary quantities of BNI exceed even the permissible N fertilizer quantities by a factor of five to ten.

In addition, Ma et al. (2021) already suggested that a strong increase in denitrification caused by the massive application of the potential BNI (linoleic acid) was most likely responsible for the observed reduction of available nitrate. Hence, clear evidence for linoleic acid to act as a BNI wasn't even delivered by Ma et al. (2021) and moreover, questioned by the authors themselves.

3.3.2 Kinds of application of BNI

Many of the BNI have a complex chemical structure (Wang et al. 2021, Subbarao et al. 2015, Coskun et al. 2017). And it is well known that generation of such biobased complex chemicals is challenging and quite expensive. Considering high BNI amounts per hectare needed for good performance (see above), costs per hectare for BNI would be so high that they would be economically prohibitively expensive for farmers. Therefore, the following major kinds of application for BNI are recommended:

- Crop rotation between BNI releasing plants (via root system) and cash crops (e.g., Wang et al. 2021)
- Intercropping of BNI releasing plants (via root system) and cash crops
- Incorporation of genes regulating BNI release (via root system) into genome of cash crops (Subbarao et al. 2021)

In case of crop rotation and intercropping it must be taken into account that the area needed to produce a comparable yield to crops treated with SNI containing fertilizers is significantly higher. And this, of course takes more time and comes along with higher fuel consumption for cultivation (and the need for a special seeding device for intercropping), finally resulting in a higher carbon oxide (CO2) footprint. In conclusion, these kinds of BNI applications are undoubtedly unsuitable for an efficient and productive crop cultivation as in Germany or Europe but probably useful for small scale farmers.

Concerning the incorporation of BNI releasing genes into plants of cash crops, it must be recalled that only classical breeding technologies (e.g., back-crossing approach) and no genetic engineering approaches are allowed/accepted at least in Germany and Europe. It must further be considered that a successful introduction of such genes by classical breeding approaches needs a lot of time. Independent from the breeding method, plant breeders need suitable rapid detection methods to evaluate the NI effect of the BNI release, and thus the breeding success.

3.3.3 Persistance of BNI in soil

However, a potential disadvantage of the inclusion of BNI releasing crops is the persistence of the BNI in the soil. Neither from a regulatory, nor from an agronomical point of view, persistence of any active ingredient (AI) applied by farmers is desired. Therefore, the full decomposition of the AI in the soil during the cropping cycle is one of the main targets in the development of SNIs. In terms of crop physiology, a long NI persistence during the crop growing period is not useful to reach high yields with high quality. For best yield performance, a mixed nutrition in the forms of ammonium (NH4) and nitrate (NO3) is better compared to N nutrition with only NH4 or NO3. With a permanent release of BNI from the roots and/or a high persistence of the BNI in the soil the nitrification process will be inhibited for a long time/the whole growing season and crops will be fed preliminary (if not solely) by high amounts of NH4, which is suboptimal for yield performance.

An optimal mixed nutrition with NH4 and NO3 is always given with SNI due to their inherently restricted time of actively inhibiting nitrification after application. Under low soil temperature (e.g., in spring), in which crop growth and so N demand is reduced, the duration of efficacy is long enough to minimize or completely exclude N (gaseous and leaching) losses from applied N fertilizers. Under high soil temperature (e.g., during growing season), the period of efficacy is shorter. The recommended dose rates of SNI consider a minimum length of action period of 3 to 4 weeks under high soil temperatures and 6 to 10 weeks under low soil temperatures.

In the case of BNI generated via plant excretions, the largest amounts of AI and thus also the strongest and longest-lasting inhibition of nitrification can be expected in phases of intensive plant growth with the best utilization of NO3 and hence, the highest demand for NO3 of the crop plants respectively. At the same time, in phases with low plant growth and high risk for N (gaseous and leaching) loss, the inhibition of nitrification would be very low or even insufficient to prevent potential N loss. As a result, BNIs do meet neither the requirements of plant production nor the requirements for reducing gaseous and leaching losses of nitrogen.

3.4 Conclusion

It is evident that the positive effects of SNI have been confirmed by various studies, including under practical conditions. Furthermore, the ecologically safe use of SNI is scientifically proven, and their usage is regulated by law and monitored by authorities. Comparable findings do not exist for the use of BNI. Moreover, the practical feasibility of BNI utilization is questionable, and its ecological safety under practical conditions, unlike SNI, is not proven. Therefore, substituting SNI with BNI while achieving similar positive effects in terms of improved NUE and reduction of GHG emissions is not possible. Contrary claims cannot be scientifically substantiated.

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