Abstract: Nerve agents (NAs) are a group of highly toxic organophosphorus compounds developed before World War II. They are related to organophosphorus pesticides, although they have much higher human acute toxicity than commonly used pesticides. After the detection of the presence of NAs, the critical step is the fast decontamination of the environment in order to avoid the lethal effect of these organophosphorus compounds on exposed humans. This review collects the catalytic degradation reactions of NAs, in particular focusing our attention on chemical hydrolysis. These reactions are catalyzed by different catalyst categories (metal-based, polymeric, heterogeneous, enzymatic and MOFs), all of them described in this review.

Keywords: Chemical Warfare Agents; catalytic degradation; metal catalysts; MOFs; enzymes

1. Introduction

Incidents involving chemical weapons, including terrorist attacks, are one of the most dangerous threats in the modern international scenario [1,2]. In fact, in the recent past, reports from the Middle East highlight the wide use of chemical weapons [3], also called Chemical Warfare Agents (CWAs) or Nerve Agents (NAs), as terrorist tool.

In general, a terrorist attack by using NAs could be performed by releasing a toxic chemical weapon in the air [4], by nebulization of the liquid or vaporization of a volatile molecule, or in water [5], by dissolving the toxic compound in the water system. In these cases, the first step will be the fast detection of the NAs [6,7], briefly shown below, followed by the prompt execution of the appropriate decontamination protocols. These protocols are based on chemical reactions by using different types of reactions, such as acid/basic conditions metal-catalyzed, polymeric/heterogeneous catalysis, enzymatic catalysis or reaction by Metal–Organic Framework (MOF). In particular, these methods allow increasing the catalytic degradation/hydrolysis rate of different order of magnitude respect to the uncatalyzed reactions. Some recent reviews summarize neutralization methods based on organocatalysts and oxidation reactions [8], polyoxometalates (POM) [8], MOF [9–12], continuous flow [8] and enzymatic reactions [13]. After a brief overview on the definition of NAs, their toxicity and detection methods, the objective of this review is to summarize the decontamination protocols able to destroy these toxic compounds, thereby restoring normal safety conditions, based on the hydrolysis reactions catalyzed by: (i) metal catalysts; (ii) polymeric/heterogeneous systems; (iii) enzymes; and (iv) MOFs [14,15]. Our attention is focused on protocols using homogeneous and heterogeneous catalytic reactions, applied both in solution and in the gaseous phase.
2. Definition of NAs

NAs are today classified into three main classes: G-type, V-type [16] and, the most recent, A-type (also called Novichok) (Figure 1) [17,18].

[Diagram showing structures and names of G-type, V-type and A-type Nerve Agents (NA)]

Figure 1. Structures and names of G-type, V-type and general formula of A-type Nerve Agents (NA) (adapted with permission from Chem. Rev. 2015, 115, PR1–PR76. Copyright 2015 American Chemical Society).

The first generation of NA, also called “G-Type” (German-agents), was discovered in the late 1930s and early 1940s. They include the Cyanophosphoramidate [19], Tabun (GA) [20] and methylfluorophosphonates compounds, such as Sarin (GB) [21], Soman (GD) [22] and Cyclosarin (GF) [23] (Figure 1).

After World War II, methylphosphothioates, called V-Type (venomous agents), were discovered: VX [24] (in Great Britain) and RVX [25] (the related Russian isomer). V-agents differ from G-agents by their lower volatility, their higher persistency in the environment and thus their higher toxicity.

All these organophosphorus (OP) compounds share a common chemical structure, in which a phosphorous (V) is bonded with a terminal oxide and three singly bonded substituents (where, in general, one is a good leaving group). For research activity, NAs cannot be used for safety and security reasons. Thus, the development of efficient catalytic degradation systems is performed by using simulants. These are organophosphorus compounds having similar chemical-physical characteristics as the NAs, but which are less reactive and thus less toxic [26,27]. The reduced toxicity can be ascribed to the absence of a good leaving group, avoiding the nucleophilic attack of the natural enzyme (vide infra). These compounds, summarized in Chart 1, can be classified into three classes: phosphonic ester (in blue), methylphosphonate (in green) and phosphothionate (in red).
Table 1 summarizes the main physical characteristics of some NAs. These compounds show volatility values comparable to water, at room temperature, thus the main method for dispersing these compounds is by aerosol, as a recent terrorist attack on the Tokyo subway demonstrated [28]. Another crucial parameter is the persistency, defined as the ability of the NA to remain active in the environment [29]. In particular, this parameter is due to the combination of the volatility, density and stability with light and water exposure. In general, as reported in Table 1, V-Type NAs show higher persistency relative to G-Type NAs due to the higher vapor pressure and volatility.

Table 1. Physical properties of NAs.

| NA          | CAS Number   | Vapor Pressure        | Volatility at 25 °C | Odor                  | Solubility at 25 °C | Persistency |
|-------------|--------------|-----------------------|---------------------|-----------------------|---------------------|-------------|
| Tabun (GA)  | 77-81-6      | 0.037 mm Hg at 20 °C  | 576–610 mg/m³       | Fruity                | 9.8 g/100 g         | T₁/₂ = 24–36 h |
| Sarin (GB)  | 107-44-8     | 2.1 mm Hg at 20 °C    | 16,400–22,000 mg/m³ | Odorless              | Miscible            | 2–24 h at 5–25 °C |
| Soman       | 96-64-0      | 0.40 mm Hg at 20 °C   | 3060–3900 mg/m³     | Fruity; oil of camphor | 2.1 g/100 g        | Relatively persistent |
| GF          | 329-99-7     | 0.07 mm Hg at 25 °C   | 59 ppm              | Odorless              | 3.7 g/100 g         | Unknown     |
| VX          | 20820-80-8   | 0.0007 mm Hg at 20 °C | 3–30.0 (10.5) mg/m³ | Odorless              | Miscible at <9.4 °C | 2–6 days   |

(Adapted with permission from Chem. Rev. 2015, 115, PR1–PR76. Copyright 2015 American Chemical Society).
3. Toxicity of NAs

The high toxicity of OP compounds is due to their rapid inhibition of AChE (Acetylcholinesterase) in the human synapses, leading to an accumulation of acetylcholine, resulting in permanent saturation of muscarinic and nicotinic receptors, which leads to cholinergic crisis [30].

The mechanism of AChE inhibition by NAs is similar to the hydrolysis of acetylcholine catalyzed by the serine–histidine–glutamate triad in the active site of the enzyme [22,31]. In the first step of the hydrolysis, nucleophilic serine attacks acetylcholine to form a tetrahedral transition state, which evolves with the release of choline (Scheme 1A). In the second step, a water molecule activated by the nearby histidine attacks the acetylserine, leading to the formation of a second tetrahedral transition state that collapses to the free enzyme and acetic acid.

In the presence of a NA compound, after reaching the active site of AChE enzyme, the OH group of serine attacks the phosphorous atom, resulting in the elimination of the leaving group (Scheme 1B). The covalent adduct is similar to the transition state of the initial step of hydrolysis of acetylcholine. However, in the second step, the histidine residue in the catalytic site cannot activate the water molecule because it is in a salt bridge with an anionic intermediate obtained after the dealkylation. For this reason, the spontaneous hydrolysis of the adduct phospho-enzyme (aged-enzyme) is extremely slow, varying from hours for dimethyl phosphoryl conjugates to days for V-agent AChE conjugates [32].

Scheme 1. (A) Mechanism of acetylcholine hydrolysis by AChE; and (B) mechanism of AChE inhibition by organophosphorus nerve agents, aging, and reactivation by oximate (adapted with permission from Acc. Chem. Res. 2012, 45, 756−766. Copyright 2012 American Chemical Society).
In the presence of a NA compound, after reaching the active site of AChE enzyme, the OH group of serine attacks the phosphorous atom, resulting in the elimination of the leaving group (Scheme 1B). The covalent adduct is similar to the transition state of the initial step of hydrolysis of acetylcholine. However, in the second step, the histidine residue in the catalytic site cannot activate the water molecule because it is in a salt-bridge with an anionic intermediate obtained after the dealkylation. For this reason, the spontaneous hydrolysis of the adduct phosphyl-enzyme (aged-enzyme) is extremely slow, varying from hours for dimethyl phosphoryl conjugates to days for V-agent AChE conjugates [32].

The presence of oximate (acting as an antidote) can prevent the dealkylation reaction due to the nucleophilic attack of the oximate anion to the phosphorous atom, leading to the phosphyloxime and restoring the natural form of the enzyme [33]. Following the reactions reported in Scheme 1, it is evident that the administration of oximate to restore the enzyme must be done as soon as possible, in order to avoid the dealkylation reaction and the “aging” of the enzyme. The aging time varies from minutes (Soman), to hours (Sarin), or days (VX and Tabun show aging time of ca. 40 h) [34–36].

The clinical manifestations after the exposure to NAs are wide [37,38]. They include salivation, lacrimation, urination, defecation, diaphoresis, gastric emesis, bronchorrhea, bronchoconstriction and bradycardia (muscarinic manifestations). Additional severe effects are related to the inhibition of nicotinic transmitters, such as fasciculations, weakness and facial paralysis. Furthermore, lethal nicotinic effects include the paralysis of the diaphragm and muscles of the chest wall.

Table 2 reports the toxicity levels of the common NAs.

| Compound | LD$_{50}$ (Percutaneous) | LC$_{50}$ | LC$_{t50}$ | IDLH [39] |
|----------|--------------------------|----------------|----------------|-------------|
| Tabun (GA) CAS#77-81-6 | 1 gm/person | 2 ppm | 100–400 mg × min/m$^3$ | 0.03 ppm |
| Sarin (GB) CAS#107-44-8 | 1.7 gm/person | 1.2 ppm | 50–100 mg × min/m$^3$ | 0.03 ppm |
| Soman CAS#96-64-0 | 0.35 gm/person | 0.9 ppm | 25–70 mg × min/m$^3$ | 0.008 |
| GF CAS#329-99-7 | 0.03 gm/person | Unknown | Unknown | Unknown |
| VX CAS#20820-80-8 | 0.01 gm/person | 0.3 ppm | 5–50 mg × min/m$^3$ | 0.002 ppm |

Nerve agents are among the most lethal agents available that have been developed for military use. The percutaneous LD$_{50}$, or dose required to kill 50% of those exposed, is in the milligram range for many agents. A drop of VX on the skin is potentially lethal. The concentration-time product is a measure of exposure to a vapor or aerosol over time. The LC$_{50}$ is the concentration-time product that is lethal to 50% of those exposed and reflects toxicity by inhalation route. IDLH is the concentration of toxin in air that is “immediately dangerous to life and health”. For VX vapor in air, 2 parts per billion is likely to result in toxicity (adapted with permission from Chem. Rev. 2015, 115, PR1–PR76. Copyright 2015 American Chemical Society).

4. Detection of Nerve Agents

In general, the detection of G- and V-type NAs is based on an instrumental method, such as ESI-MS [40], HPLC-MS [41] or GC-MS [42]. These techniques are very sensitive and selective, but have the disadvantage of not being able to be performed in real-time, due to instrumental dimensions. An efficient alternative detection method is based on “molecular sensors”, in which a molecule reacts/interacts with the analyte, giving a change of a measurable response (i.e., electrical, optical or magnetic response) [43]. In this context, NAs detection via molecular sensors is based on a “covalent approach”, in which a covalent reaction occurs between the sensor and the analyte, leading to the formation of a new compound having different properties with respect to the starting sensor (Figure 2A) [44]. In particular, detection methods based on spectroscopic measurements (e.g., optical measurements, such as absorbance or fluorescence) are cheap and convenient, due to fast and clear
visible responses to the presence of the analyte [45]. However, the covalent approach suffers from certain limitations: (1) low selectivity, due to the possibility of reaction with other substances; and (2) one-time use, due to the covalent and irreversible reaction with the analyte.

![Diagram A: Covalent bond](image1)

![Diagram B: Lewis acid-base interaction, CH-\(\pi\) interaction, Hydrophobic interaction, Hydrogen bond](image2)

**Figure 2.** (A) Covalent approach; and (B) supramolecular approach used with chemical sensor for the detection of NAs.

Recently, an alternative detection method based on the formation of non-covalent interactions between the sensor and the analyte has been proposed. Due to the nature of these non-covalent interactions, this strategy is called “supramolecular approach” [46]. The goal of the supramolecular approach is to give alternative pathways with respect to the traditional chemical reactivity, minimizing or eliminating the effects due to the presence of competitive analytes, leading to a reusable sensor. In fact, the formation of non-covalent interactions leads to a reversible complex with the analyte [47–59].

In this context, by taking advantage of the most recent findings in the field of supramolecular chemistry, sensing devices for the non-covalent detection of CWA molecules via a “multi-topic approach” have been synthesized [60–65]. In particular, the target is to recognize CWAs via non-covalent reversible interactions, involving different recognition sites (multi-topic) of the analyte. The possibility of simultaneously recognizing two or more sites of the analyte leads to highly efficient and selective sensors, avoiding false-positive responses (Figure 2).

5. Chemical Hydrolysis

5.1. Metal-Catalyzed Hydrolysis

The catalytic systems described in this paragraph can be rationalized by use of two possible reaction mechanisms: a mono-metallic and a bi-metallic mechanism (Scheme 2). In many cases, the bi-metallic mechanism is utilized, simulating the catalytic activity of enzymes, where more than one Lewis acid center is present in the active site.
Scheme 2. Hydrolysis or methanolysis by mono-metallic or bi-metallic mechanisms (adapted with permission from Chem. Rev. 2015, 115, PR1–PR76. Copyright 2015 American Chemical Society).

Moss et al. reported the chemoselective metal-catalyzed hydrolysis of some phosphonoformate diesters (Chart 1, Compounds 1–4) [66]. Hydrolytic reaction occurs due to the Lewis acid activation of the substrate by coordination with the metal ion and subsequent reaction with a water/hydroxyl group coordinated with the metal catalyst. In this case, a bimetallic mechanism is invoked. In particular, the two metal centers coordinate two oxygen atoms of the phosphoric group, and a hydroxyl group (initially bonded to the metal catalyst) attacks the organophosphorus substrate leading to the hydrolysis.

In addition, the chemoselectivity is due to the different metal ions able to hydrolyze different bonds: the ester bond C-OR is cleaved by Ce(IV) and Th(IV), while phospho-ester bond is cleaved by Zr(IV) and Hf(IV). In both cases, the authors detected the same leaving groups (–CH₃ or –Ph).

To understand the hydrolytic mechanism, they consider an intermediate where the selectivity of Zr(IV) and Hf(IV) toward phospho-ester bond is due to the formation of octameric or tetrameric complexes between the metal ion and the substrate. In some cases, such as with compound 3, C-OPh ester bond hydrolysis occurs with respect to P-OMe, due to the modification of the catalyst-substrate complex geometry.

Lewis et al. reported the methanolysis of the methylphosphonate compounds 5–10 (see Chart 1), by using La³⁺ and Zn²⁺ complexes [67].

A comparison of the reactivity between phosphonate and phosphate triesters shows that the former are ca. 100-fold more reactive than the latter, also containing the same leaving groups. The catalysis is highly efficient, although in mild conditions (near to neutrality). Reaction occurs due to the activation of the substrate by Lewis acid-base interaction, followed by the methoxide attack to the phosphorous center.

The most reactive compound is methylphosphonate 5, in which the acceleration rate depends on the alkaline conditions (in the range ca. 10⁶–10⁷-fold). Conversely, the least reactive compound is methylphosphonate 10, with an increase of the rate of ca. 10⁴–10⁵-fold.

Brown and co-workers applied the same reactions to phosphonothioate compounds 17–21, obtaining good results in terms of acceleration rates at room temperature and pH values [68].

Notably, the authors describe that a VX analogue can be methanolyzed at 25 °C in the presence of 1 mM of La³⁺ catalyst with a t₁/₂ less than 1 s.
Kuo et al. reported the catalytic degradation of O,S-diethyl phenylphosphonothioate 22 (DEPP, Chart 1), a simulant of neurotoxins, including VX, in mild conditions by using a metallocene catalyst (bis(η5-cyclopentadienyl)molybdenum(IV) dichloride, Cp₂MoCl₂) [69]. The authors proposed a mechanism in which the substrate coordinates the metal catalyst by using both P=O and S atoms, thus activating the nucleophilic attack of a water molecule (or OH⁻ in alkaline conditions) to the phosphorous metal center, with a mechanism very similar those reported in Scheme 2 (monometallic catalyst). Faster reactions were obtained increasing the electrophilicity of the metal center, by introducing in the cyclopentadienyl ligand two methyl groups.

Singh and et al. reported a micellar system, by self-assembly of benzimidazolium receptor and an anionic surfactant (Scheme 3A), able to detect, by fluorescence measurements, the presence of the NA (diethylchlorophosphate, DCP) which then led to its degradation into non-toxic diethylhydrophosphate (DHP) (Scheme 3B) [70].

The benzimidazolium receptor is able to recognize DCP by non-covalent interactions (Scheme 3B), leading to a strong turn-on of the emission due to an increase of the rigidity of the complex with DCP with respect to the starting sensor. The formation of the host–guest complex leads to the activation of the P=O group, due to the formation of a strong hydrogen bond. The degradation reaction was monitored by GC-MS, forming tetraethyldiphosphate (TDP) as an intermediate, which completely evolves into DHP in 1 h.

5.2 Polymeric/Heterogeneous Hydrolysis

Chang et al. reported the synthesis of a polymer based on TRIM building block, containing copper as the metal-center catalyst and its catalytic activity towards the hydrolysis of some phosphate esters (Scheme 4) [71].
The benzimidazolium receptor is able to recognize DCP by non-covalent interactions (Scheme 3B), leading to a strong turn-on of the emission due to an increase of the rigidity of the complex with DCP with respect to the starting sensor. The formation of the host–guest complex leads to the activation of the P=O group, due to the formation of a strong hydrogen bond. The degradation reaction was monitored by GC-MS, forming tetraethyldiphosphate (TDP) as an intermediate, which completely evolves into DHP in 1 h.

Scheme 3. (A) Schematic representation of micellar assembly, able also to recognize DCP; and (B) catalytic hydrolysis of DCP.

5.2. Polymeric/Heterogeneous Hydrolysis

Chang et al. reported the synthesis of a polymer based on TRIM building block, containing copper as the metal-center catalyst and its catalytic activity towards the hydrolysis of some phosphate esters (Scheme 4) [71].

Scheme 4. (A) Synthesis and chemical structure of Cu-TRIM catalyst; (B) substrates tested; and (C) mechanism of hydrolysis.

In particular, hydrolysis of NPP, BNPP and MEP (Scheme 4B) was accelerated by the polymeric catalyst of 580, $2.5 \times 10^4$ and $6.7 \times 10^5$-fold, respectively, with respect to the uncatalyzed reaction. As reported in Scheme 4C, firstly the substrate coordinates the metal ion by removing a water molecule, then the intramolecular nucleophilic attack by a second water molecule bonded to the metal ion occurs, thus leading to a four-member cycle, which undergoes the elimination of the alkoxide substituent. Further reorganization of the cyclic intermediate leads to the hydrolysis product, recovering the starting catalyst. Thus, this polymer represents an efficient heterogeneous catalyst able to hydrolyze phosphate esters.

Brown et al. reported the methanolysis of some phosphor-esters (Compounds 6, 17, 23 and 24 in Chart 1) catalyzed by solid support containing lanthanide ions (La$^{3+}$, Sm$^{3+}$, Eu$^{3+}$ and Yb$^{3+}$), in alkaline conditions [72].

Solid supports have been synthesized starting from commercial chlorobenzyl silica gel and polystyrene functionalized with iminodiacetic acid (IDA) and ethylenediamine-$N,N'$-diacetic acid (EDDA), in the presence of Ln$^{3+}$ metal ions. With respect to the uncatalyzed reactions in the presence of methoxide anion, hydrolysates of 6 and 23 are about $8.5 \times 10^5$- and $1.76 \times 10^6$-fold faster, respectively. Similarly, increase of the reactions with 17 and 24 are $6.3 \times 10^5$- and $5 \times 10^8$-fold with respect to the uncatalyzed reactions. Solid catalysts containing Eu and Yb ions have been recycled many times without loss of reactivity. Based on the previous work [73], the authors proposed a monometallic mechanism, as summarized in Scheme 2. In the first step, the substrate coordinates metal center by Lewis acid-base interaction, thus activating the P=O group, then a nucleophilic attack of the methoxide to the P atom occurs, leading to a four-member ring, which results in the releasing of hydrolyzed organophosphorus product restoring the catalyst by addition of methanol (solvent).

5.3. Enzymatic Hydrolysis

Hydrolitic enzymes (organophosphorus hydrolase) can catalyze the hydrolysis of NAs, however the main limitation is related to the decrease of the pH of the reaction environment, due to the acidic nature of the hydrolysis products (for example, most of G-Type NAs release HF after the hydrolysis). In general, enzymatic efficiency decreases at pH values of $< 6$ [74].

To avoid this problem, buffers may be used to maintain a neutral pH. In addition, some enzymes lead to the formation of ammonia starting from urea and can be used to control the pH levels [75].
In this way, by combining the two enzymes, organophosphorus hydrolase to hydrolyze the NA and urease to maintain the pH conditions, good conversion values can be obtained without loss of efficiency.

Enzymatic hydrolysis also exhibits the problem of the transport of the NA into the active site of the enzyme. To overcome this problem, catalytic enzymes have been anchored onto the surface of bacteria, and the whole system has been exposed to the NA. In particular, Mulchandani et al. reported on the coupling of DNA able to codify the organophosphorus hydrolase enzyme to the DNA able to codify some proteins of the cell surface [76]. With this strategy, several bacterial lines which have the catalytic enzyme on their surface can be obtained.

Following the same methodology, Mulchandani et al. also developed engineered E. coli bacteria, which have a cellulose-binding domain on the cellular surface, in order to create a reactor based on common fibers containing these nanocatalysts (Figure 3) [77]. This system was employed to catalyze the paraoxon hydrolysis in seven weeks, with the device being reused 15 times.

![Figure 3. Schematic representation of the reactor based on cellulose nanocatalyst (reproduced with permission from Biotechnol. Bioeng. 2005, 91, 379–386. Copyright 2005 John Wiley and Sons).](image)

In addition, several different classes of enzymes are able to hydrolyze organophosphorus compounds. In particular, Phosphotriesterases (PTE), containing a binuclear zinc or cobalt center in the active site, catalyze the hydrolysis of Sarin, Soman, Tabun and Cyclosarin, as well as VX and VR [78,79]. Furthermore, Serum paraoxonase 1 (PON1), a mammalian calcium-dependent lactonase/arylesterases, is able to hydrolyze G-Type NAs [80–82]. In addition, Diisopropyl-fluorophosphate fluorohydrolase (DFPase) hydrolyzes Tabun, Soman and Sarin [83]. Recently, Phosphotriesterase-like lactonase (PLL) enzymes have been discovered to hydrolyze some OP, and in particular cyclosarin [84].

5.4. Hydrolysis by MOFs

MOFs are a new class of porous nanomaterials. They present high surface area and internal volume, suitable for many interesting applications [9–13,85–103]. Building blocks are metal ions, having different coordination geometries, and a large range of organic ligands. For this reason, a wide typology of structures can be obtained [104–111].
Due to their three-dimensional structures, these nanoscopic compounds can be used as sensors for small and large molecules. The typical characteristics of MOFs are the extensive surface area (up to 1000 m²/g), the huge number of reactive sites having potential catalytic activity, the possibility to regulate the pore sizes and the inner volume (by using different metal ions and organic ligands), and tuning the catalytic properties regulating the nature of the metal ions.

Catalytic hydrolyses of NAs by MOFs are inspired by the enzyme-catalyzed hydrolysis of phosphor-ester substrates, in which a Zn ion leads to the activation of the P=O group, facilitating the nucleophilic attack of the water molecule. In this context, Kats et al. reported the synthesis of based biomimetic MOFs containing Zr, able to hydrolyze NAs, in particular the methyl paraoxon and p-nitrophenyl diphenyl phosphate [112]. Similarly, Wagner and Peterson reported on the ability of a copper-based MOF (CuBTC) to hydrolyze VX and Soman in a matter of hours [113].

More efficient systems have been synthesized. Nunes and co-workers prepared UiO-67 MOF able to degrade ca. 90% of Sodium para-nitrophenylphosphate (a simulant of Soman) by simple filtration of NAs solution through the MOF [114].

Farha and co-workers synthesized different MOFs, tuning the linker between the metal center [115]. They established that the linker size and functional groups (amine or alkylamino) can strongly modulate the reactivity towards the hydrolysis of the NA. In particular, hydrolysis of 4-nitrophenylphosphate buffered at pH 10 occurred in only a few minutes by using the smaller MOFs containing amino groups in the linker. The reaction was monitored by using NMR and UV–Vis spectroscopies. In addition, the authors tested the catalytic degradation of Soman but, in this case, the reaction is too much fast to obtain information on the effect of the substituent of the MOF linker.

Recently, the same research group developed a composite material, integrating MOFs into a polymeric matrix (linear polyethylenimine), able to efficiently destroy DMNP and GD in mild conditions in the presence of an organic volatile base (N-ethyl morpholine), obtaining a solid device suitable for the decontamination from NAs (Figure 4) [116].

![Figure 4. (A) Representation of MOF-808, PEI and image of the composite; and (B) degradation reaction of DMNP (adapted with permission from J. Am. Chem. Soc., 2019, 141, 20016–20021. Copyright 2019 American Chemical Society).](image)

In particular, the authors demonstrated that the MOF pores contain only water molecules during the catalytic process, highlighting higher activity with respect to the other MOF systems in a water environment. Robustness and durability have been demonstrated, by stirring the sample in water for 24 h, observing the maintaining of the crystalline structure and the quantitative composition.
Furthermore, the catalytic properties are retained following storage in air for 100 days. In addition, scalability of the system was tested with good results, by testing a larger surface of the device.

Cohen et al. described a library of 26 UiO-66 derivatives, combining five different ligands, leading to Multivariate MOF catalysts (MTV-MOFs), able to hydrolyze DMNP in basic conditions (pH = 8) [117]. These MTV-MOFs have been synthesized by including nine different ligands into a single MOF structure. MTV-MOF catalysts show higher efficiency with respect to the mixture of single MOFs in the degradation of DMNP (Figure 5). In particular, this new type of nanocatalysts is more efficient than MOFs containing the same ligand. However, the authors did not find a correlation between the electron nature of the substituent in the ligand (electron-donating or withdrawing) and the catalytic efficiency. We note that, in analogy with what was previously observed [115], the best results of catalytic efficiency have been found by using ligands containing amino and bromide groups.

Figure 5. Chemical structure of the ligands employed to synthesize MTV-MOFs and hydrolysis rates of MTV-MOFs (in blue) and physical mixture of MOFs containing the same ligand (in red) (adapted with permission from Chem. Commun. 2019, 55, 5367–5370. Copyright 2019 Royal Society of Chemistry).

6. Conclusions and Future Perspectives

Catalytic degradation methods of NAs by using molecular catalysts, both in homogeneous and heterogeneous conditions, enzymes and MOF systems are summarized. In most of the examples, simulants of NAs have been employed. This is for security reasons: as the use of real NAs is not allowed in most research laboratories, these tests are made with organophosphorus compounds having similar chemical characteristics with respect to the NAs. However, recently, DeCoste and Ploskonka focused their attention on the use of simulants against the real NAs in the study of hydrolysis processes [118]. They found that the reactivity of these simulants is not always comparable to the reactivity of the NAs, in particular by using nanoporous MOFs. In fact, they supposed that the reactivity inside the MOF structure is not only related to chemical interactions, but also steric factors should be considered. NAs show steric hindrance which, in many cases, differs with respect to that of the simulant used. However, these considerations are relative to the catalytic systems having restricted steric hindrances.

Due to the fast action mechanism of NAs to covalently bind AChE, the rate of NA degradation is a crucial parameter in order to avoid the lethal effects of these chemical weapons to the humans. For this reason, the implementation of molecular catalytic systems into heterogeneous of nanoscopic catalysts could be the goal to obtain efficient decontamination of the environment. As is well known, the possibility to realize solid porous surface/support containing a catalytic specie leads to an increase of the activity/reactivity, also obtaining a reusable device [119–121]. Scientific progresses in the field of...
surfaces and nanoparticles functionalization improves the possibility of enhancing the results actually obtained with regard to NAs degradation.

Today, impressive research activity in material sciences, as well in nanoscience and enzymology leads to a greater chance of obtaining practical devices able to efficiently destroy nerve agents. In addition, the possibility of using these devices in public environments (such as airports, stations, schools and water systems) can potentially increase safety and security in protecting against terrorist attacks.

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