A review of advances in the detection of sulfur mustard based fluorescence

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Abstract. Sulfur mustard is a vesicant through alkylating that have a garlic-like odor. As extreme toxicity, there has an increased demand to develop effective systems for the detection of sulfur mustard. This review described the research progress of chemical sensors based on fluorophore for the detection of sulfur mustard and its mimic. Focusing on current developments in fluorescence approaches has been used for detection of sulfur mustard, especially approach offers rapid, low limitation, low-cost, real-time and on-site visual detection capability.

1. Introduction

Chemical Warfare Agents (CWAs) can be classified on toxic effectiveness. They can be divided into five categories, including never agents, systemic toxic agents, choking agents or suffocating gas, blister agents or vesicants and incapacitating agent. Surfur mustard (bis(2-chloroethyl) sulfide, CAS No.505-60-2) also known as mustard gas is an extreme toxicities vesicants. The Acute Exposure Guidance Levels (AEGLs) focus on the short-term effects of mustard gas exposure concentrations and durations, ranging from 10 minutes to 8 hours of acute exposure.[1]. Sulfur mustard with the concentration at the AEGL-1 level is 0.40 mg/m 3 to an exposure duration of 10 min[2]. There is no specific antidote for the symptoms of sulfur mustard[3, 4]. From World War Ⅰ to the Iran-Iraq conflict, sulfur mustard had been introduced as a warfare agent and used extensively. In Iran-Iraq war, sulfur mustard resulted more than 100,000 chemical casualties[3]. Fluorophore-based chemosensors function on the basis both or either one of absorption and fluorescence intensity changes that accompany chemical reactions with sulfur mustard.[5-10].

In fluorescence probe for detection of chemical warfare agents, the target analytes focus on phosgene and nerve agents. The reaction moiety in the recent literature for phosgene and nerve agents, include amine[11], pyridine[12], hydroxyl[13, 14], oxime[15, 16], o-phenylenediamine[17, 18]. In recent years, the design ideas of fluorescent probe for the detection of sulfur mustard mainly focus on its strong electrophilic ability. Amine group, as a reaction group with a relatively strong nucleophile, was also used in the detection of alklylation reagents including sulfur mustard(Figure 1a)[19]. Nevertheless, nerve agents and phosgene are also highly electrophilic, that may cause large interference with the selectivity of these probes. The approaches established for sulfur mustard have mainly targeted electrophilic and hydrogen bond sites. Therefore, the fluorescent probes with sulfur as the reaction site have gained more and more recognition for detection sulfur mustard[20-27].
2. Sulfur mustard fluorescence probe based on dithiol
In 2013, V. Anslyn and co-workers developed a series of fluorescence probe based on dithiol for detection sulfur mustard[26, 28]. Finger 1b, the dithiol reacted with sulfur mustard simulant to form a podand-type compound, further react with Cd$^{2+}$ to give a turn-on of fluorescence. This method can effectively anti-interference of electrophilic reagent and high selectivity for sulfur mustard. At 80°C addition of sulfur mustard to pH=9 solution, the response time was 1 min and the limit of detection 200 µM.

Finger 1c, the chemosensing solution would be changed fluorescence and color by the dithiol with squaraine dye reversible reaction. In the presence of sulfur mustard simulator, the squaraine dye exhibit characteristic color and fluorescence utilizes dithiol reaction generates podand-type compound. The probe limit of detection for sulfur mustard is 10 µM, and provides a strategy for sensitive and selective monitor.

![Figure 1. Structure of fluorescence probe](image1)

3. Sulfur mustard fluorescence probe based on metal nanoparticles
D. Beer and co-workers designed a dansyl fluorophore ligated to gold nanoparticles to detect sulfur mustard in 2013[20], in figure 2. The dansyl fluorophore were connected to the gold nanoparticles by imidazole and amine groups. In the present of sulfur mustard, nanoparticles via surface energy transfer switch-on fluorescence sensing response.

![Figure 2. The ligands of gold nanoparticle](image2)

4. Sulfur mustard fluorescence probe based on rhodamine-thioamide
The rhodamine scaffold have a high fluorescence quantum yield after spirolactam ring-opened. Pardasani and co-workers developed the rhodamine-thioamide based sulfur mustard sensors (Figure 3a)[21]. After thioamide reaction with sulfur mustard, the spirolactam ring-opened and the fluorescence increase about 100 times. The probe is highly selective for otential DNA alkylating agents include sulfur mustard, the limit of detection in solution is 4.75 µM. Based on a similar spirolactam ring-opened concept, Wang and co-works designed a fluorescent chemosensors for sulfur mustard (Finger 3b)[29].
Figure 3. Sulfur mustard fluorescence based on rhodamine-thioamide

5. Sulfur mustard fluorescence probe based on thione
The thione as the reactiong moiety based on fluorescence dye skeleton was developed for detection of sulfur mustard by V. Kumar and co-works[27]. Upon exposure to sulfur mustard, the thione moiety sulfur alkylation reaction leads to the generation of the highly fluorescent (figure 4a). The synthesis of probe was realized in a single step, and colorimetric and fluorescent sensor for the detection of sulfur mustard. The probe appeared a distinctive color can be observed by naked-eye and hand-held UV lamp with the concentration of 0.04 mg/mL.

Based on a similar molecular S-alkylation reaction, Tian and co-workers designed a xanthene molecular skeleton a highly selective nucleophilic reaction with sulfur mustard simultant (figure 4b)[25]. The limit of detection for sulfur mustard simultant is 1.2 µM in solution and 0.5 ppm in the gas under room temperature. Sulfur is used to replace the oxygen on the carbonyl moiety of the fluorophore group to quench the fluorescence. In the presence of sulfur mustard simultant, upon thione s-alkylation the probe's fluorescence quantum yield is tremendous increased from 0.002 to 0.53 and led up to 850 fold fluorescence signal.

Figure 4. Structure of molecules utilizing thione.

6. Conclusion
Sulfur mustard is a high toxicity blister agents. It was used in war would lead to a serious threat to nation security. According to statistics, the current number caused by sulfur mustard outnumber the total sum due to all other chemical agents[30]. Although there are some advances made in the design of fluorescence probe for sulfur mustard, several challenges and problems still exist for future studies, especially in the practical application.

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