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Biological and Pharmaceutical Organosulfur Molecules

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ABSTRACT

Organosulfur molecules are prevalent in a broad spectrum of active biological, pharmaceutical and natural molecules. In this category, compounds containing carbon–sulfur bonds occupy a very special place in chemistry science. In this paper, we focused on biologically and pharmaceutically active molecules containing sulfides, disulfide, sulfoxid, sulfone, thiosulfinate, thioester and trithiocarbonate scaffolds. Methionine, Cystine, Pantoprazole, Dapsone, Allicin and Acetyl Co-A are several organosulfur molecules with well-known biological and pharmaceutical activities.

1. Introduction

Sulfur chemistry, which encompasses sulfur-containing compounds or organic sulfur compounds, is an integral part of chemical and medicinal science and plays a substantial role in the current research in these areas, in particular organic synthesis.[1-2] Sulfur-containing compounds are prevalent in a broad spectrum of active biological, pharmaceutical and natural molecules.[3-4] In this category, compounds containing carbon–sulfur bonds occupy a very special place in chemistry science. Carbon-sulfur bonds are prevalent in a wide range of compounds that have significant biological, pharmaceutical, industrial and/or materials properties.[5-7] The synthesis of pharmaceutical active sulfur molecules inevitably needs to form of C–S bonds.[1] Due to the high importance of these compounds, in this paper we provided a scientific effort to list the compounds containing carbon–sulfur bonds reported in the literature and studied their biological, pharmaceutical and industrial activities.

2. Classification

A series of organo-sulfur compounds containing C–S bonds are shown below.

2.1. Sulfides

Sulfides, formerly known as thioethers, are characterized by C−S−C bond. Sulfides are typically prepared by alkylation of thiols.[1] The far-reaching chemistry of sulfides attracts specific attention in organic synthesis primarily because of its terrific significance in nature and medicine.[1] Thioethers are very effective in the treatment of various diseases such as cancer, leprosy, Alzheimer's, Parkinson, tuberculosis, and HIV.[1-3] Sulfides are integral and supplementary parts of are integral and supplementary parts of many biological active molecules and antibiotics such as cysteine derivatives, penicillins, nucleoids, and proteins.[1] Some these compounds are listed below:

Thiethylperazine**:** It is a dopamine antagonist that is particularly useful in treating the nausea and vomiting associated with anesthesia, mildly emetic cancer chemotherapy agents, radiation therapy, and toxins (Fig. 1).[8]

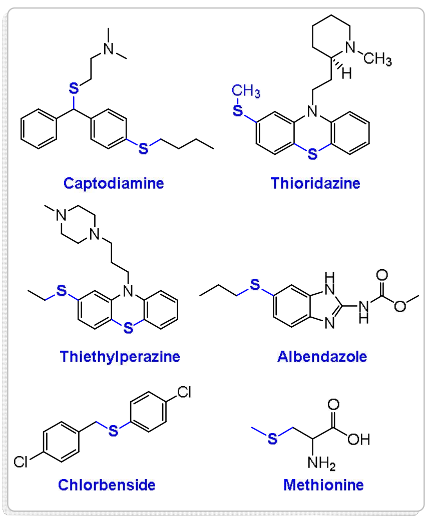

Fig 1. Pharmaceutical and biological active molecules containing sulfide scaffolds.

Albendazole**:** It is a medication used for the treatment of a variety of parasitic worm infestations. It is useful for giardiasis, trichuriasis, filariasis, neurocysticercosis, hydatid disease, pinworm disease, and ascariasis (Fig. 1).[9]

Captodiamine: It is an antihistamine which is used as a sedative and anxiolytic (Fig. 1).[10]

Thioridazine**:** It is a phenothiazine antipsychotic used in the management of psychoses, including schizophrenia, and in the

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control of severely disturbed or agitated behavior (Fig. 1).[11] Chlorbenside: It is a pesticide and as an acaricide being most commonly used to kill mites and ticks (Fig. 1).[1]

Methionine: It is a dietary essential amino acid that plays unique roles, both in protein structure and in metabolism. Methionine serves as the initiating amino acid in eukaryotic protein synthesis (Fig. 1).[12]

2.2. Disulfides

Compounds containing sulfur–sulfur (S–S) bonds, often called disulfides or more specifically disulfanes, are arguably one of the most important classes of organosulfur compounds.[13] Oxidative coupling of thiols is popular strategy for the preparation of organic disulfides.[13] Disulfides are very important in nature because they possess a high potential to stabilize the folded form of proteins.[13]

Disulfides are readily constructed via covalent links between parts of a polypeptide molecule or between two polpeptide links or strings.[13-15] In proteins, S–S bonds often stabilize the secondary and tertiary structure.[13] The accurate formation of S–S bonds is important, because their inaccurate formation leads to protein aggregation and subsequent degradation by cellular protease.[16-19] Disulfides exist in the structural backbones of a wide range of natural biologically important molecules such as peptides, oligonucleotides, enzymes, and nucleic and amino acids.[20-22] Some these compounds are listed below:

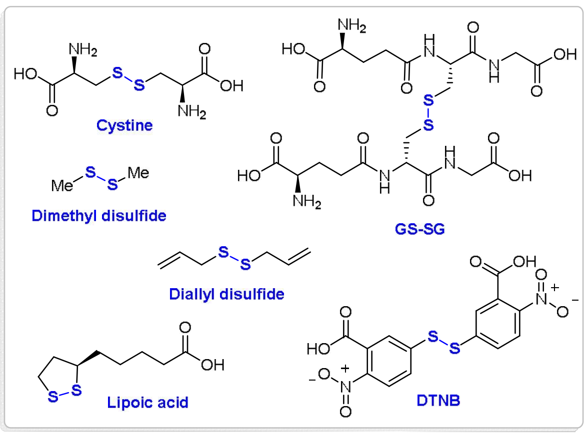

Fig 2. Pharmaceutical and biological active molecules containing disulfide scaffolds.

Cystine: It functions as an antioxidant and protects tissues against radiation and pollution, slowing the aging process. It also aids protein synthesis. Cystine is abundant in many proteins of skeletal tissues and skin (Fig. 2).[13]

Glutathione disulfide: Ii is a very important and valuable molecule from a biological perspective. It has been shown to protect mice against acetaminophen-induced hepatotoxicity (Fig. 2).[13] Lipoic acid: It is a vitamin-like antioxidant that acts as a free-radical scavenger. It is a naturally occurring compound that is synthesized by both plants and animals (Fig. 2).[13]

Diallyl disulfide: It is well-known molecules due to its notable biological properties such as antimicrobial and insecticidal (Fig. 2).[13]

Dimethyl disulfide: It is a food additive, sulfiding agent, and an effective soil fumigant in agriculture (Fig. 2).[13]

Ellman's reagent: It is commonly employed for the estimation of free thiol groups on proteins (Fig. 2).[13]

2.3. Sulfoxides

Sulfoxide, a class of organic compounds containing sulfur and oxygen and having the general formula (RR′) SO, in which R and R′ are a grouping of carbon and hydrogen atoms. The oxidation of sulfides is the most straightforward strategy for the preparation of the sulfoxides.[24-25] Sulfoxides are good solvents for salts and polar compounds. The best-known sulfoxide is dimethyl sulfoxide (DMSO), which is a key dipolar aprotic solvent.[26] Sulfoxide derivatives are also prevalent structural motifs in many drugs and biologically active molecules.[24-28]

A nice category of valuable pharmaceutical and biological molecules containing S=O bonds are listed below:

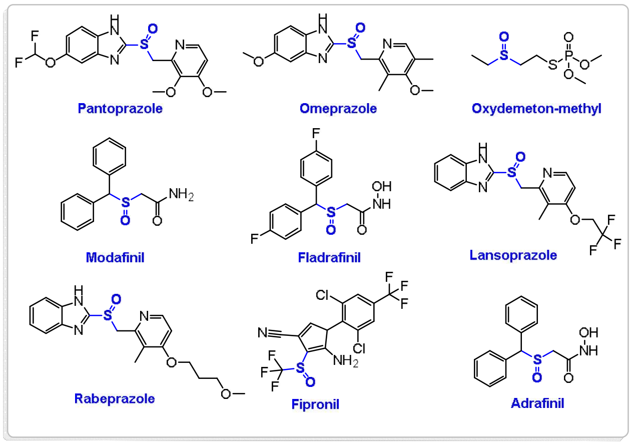

Fig 3. Pharmaceutical and biological active molecules containing sulfoxide scaffolds.

Modafinil: It is used to treat a lot of sleepiness that may happen with sleep apnea, narcolepsy, or shift work problems (Fig. 3).[29]

Adrafinil: It acts as a central nervous system stimulant, preventing fatigue and increasing energy and wakefulness (Fig. 3).[30]

Fladrafinil: It is a synthetic nootropic and concentration drug which is chemically similar to adrafinil and modafinil (Fig. 3).[31]

Fipronil: It is used as the active ingredient in flea control products for pets and home roach traps as well as field pest control for corn, golf courses, and commercial turf (Fig. 3).[32]

Oxydemeton-methyl: It is primarily used to control aphids, mites, and thrips (Fig. 3).[33]

Omeprazole: It is used to treat certain stomach and esophagus problems (such as acid reflux, ulcers). It works by decreasing the amount of acid your stomach makes (Fig. 3).[34]

Pantoprazole: It is used for short-term treatment of erosive esophagitis associated with gastroesophageal reflux disease (GERD), maintenance of healing of erosive esophagitis, and pathological hypersecretory conditions including Zollinger–Ellison syndrome (Fig. 3).[35]

Lansoprazole: It is used to treat gastroesophageal reflux disease (GERD), a condition in which backward flow of acid from the stomach causes heartburn and possible injury of the esophagus (the tube between the throat and stomach) (Fig. 3).[32]

2.4. Sulfones

A sulfone is a chemical compound containing a sulfonyl functional group (SO_2) attached to two carbon atoms. The oxidation of sulfides is perhaps still the most favored method for the synthesis of sulfones. Sulfones are versatile synthetic intermediates in organic chemistry, and molecules bearing a sulfone unit have found various applications in diverse fields such as agrochemicals, pharmaceuticals and polymers.[36-37] A large number of biologically active molecules contain this functional group.[38]

A nice category of valuable pharmaceutical and biological molecules containing SO_2 bonds are listed below:

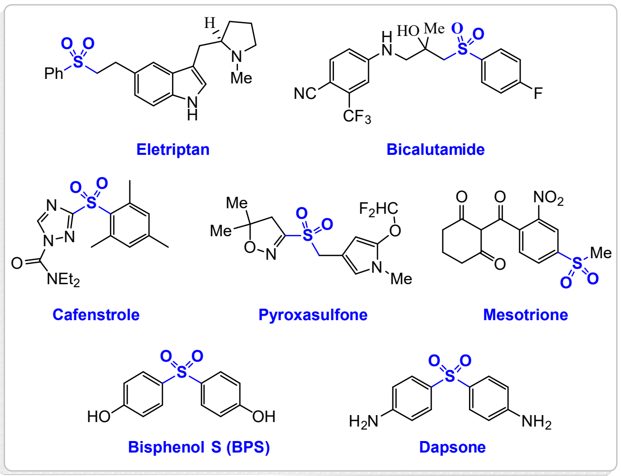

Fig 4. Pharmaceutical and biological active molecules containing sulfoxide scaffolds.

Eletriptan: It (trade name Relpax, used in the form of eletriptan hydrobromide) is a second generation triptan drug intended for treatment of migraine headaches. Eletriptan is used as an abortive medication, blocking a migraine attack which is already in progress (Fig. 4).[39]

Bicalutamide: It is an oral medication that is used for treating cancer of the prostate (Fig. 4).[39]

Dapsone: It is an antibacterial in the sulfone family of antibiotics, which is used to treat leprosy and the skin condition known as dermatitis herpetiformis (Fig. 4).[39]

Mesotrione: It is a new selective herbicide for use in maize (Fig. 4).[39]

Pyroxasulfone: It is a new herbicide that has been registered for use on major crops including corn and soy (Fig. 4).[39]

Cafenstrole: It is used for the pre- and early post-emergence control of annual weeds, particularly grassy weeds in paddy fields (Fig. 4).[39]

Bisphenol S (BPS): BPS is used in curing fast-drying epoxy glues and as a corrosion inhibitor. It is also commonly used as a reactant in polymer reactions (Fig. 4).[39]

2.5. Thiosulfinate

Thiosulfinate or Thiosulfinate ester is a functional group consisting of the linkage R-S(O)-S-R (R: are organic substituents). A variety of acyclic and cyclic thiosulfinates are found in plants, or formed when the plants are cut or crushed. Thiosulfinate esters are recognized to have significant and wide biological activities.[40]

The natural products allicin and leinamycin are thiosulfinate esters. These species were reported to have antibacterial, antineoplastic, antifungal, antithrombic, hepatoprotective, and cholesterol-lowering properties.[41] Allicin (Fig. 5), well-known for its potent antimicrobial activity, is a popular molecule under investigation for its medicinal potential to treat diseases such as cardiovascular and neurodegenerative diseases.[41-42]

2.6. Thioesters

Thioesters are compounds with the functional group R–S–CO–R. The esterification of thiols is the most common and popular reaction for the preparation of thioesters derivatives. The S-acylation of thiols also provides an effective and inexpensive strategy to protect sulfhydryl groups in multistep synthesis of natural products, biological and pharmaceutical active molecules.[5]

Thioesters are valuable intermediates in food, chemical, medicinal and cosmetic industry.[5] These compounds also participate in the synthesis of a number of other cellular components, including peptides, fatty acids, sterols, terpenes, porphyrins, and others.[5]

The best-known thioesters are derivatives of coenzyme A and acetyl coenzyme A. Acetyl coenzyme A (Fig. 5), or better known as acetyl-CoA, is an important molecule used in metabolic processes.[43] It is primarily used by the body for energy production through the citric acid cycle, or Krebs cycle.[43]

2.7. Trithiocarbonates

Trithiocarbonates (Fig. 5), are an important class of compounds containing C–S bonds which have received considerable attention due to their tremendous industrial, synthetic, and medicinal applications.[2]

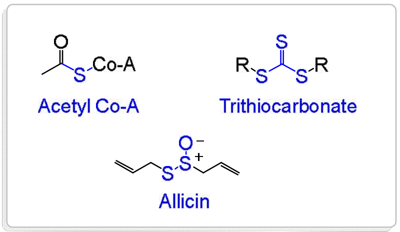

Fig 5. Pharmaceutical and biological active molecules containing thiosulfinate, thioester and trithiocarbonate scaffolds.

Trithiocarbonate derivatives are used to as inhibitors in the treatment of cancer, and as pesticides in agriculture, lubricating agents in oil additives and materials science.[2] They have also reported as chain transfer agents for reversible addition fragmentation chain-transfer (RAFT) in free radical polymerization processes.[2]

3. Conclusion

As illustrated in this paper, compounds containing carbon–sulfur bonds are very vital especially in the arena of pharmaceutically and biologically active compounds. The described examples clearly showed the high importance of organosulfur molecules in medicinal and chemical science. We hope to make greater achievements in this field in the near future.

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