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REVIEW

Sulfonamide drugs: structure, antibacterial property, toxicity, and biophysical interactions

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Abstract

Sulfonamide (or sulphonamide) functional group chemistry (SN) forms the basis of several groups of drug. In vivo sulfonamides exhibit a range of pharmacological activities, such as anti-carbonic anhydrase and anti-t dihydropteroate synthetase allowing them to play a role in treating a diverse range of disease states such as diuresis, hypoglycemia, thyroiditis, inflammation, and glaucoma. Sulfamethazine (SMZ) is a commonly used sulphonamide drug in veterinary medicine that acts as an antibacterial compound to treat livestock diseases such as gastrointestinal and respiratory tract infections. Sulfadiazine (SDZ) is another frequently employed sulphonamide drug that is used in combination with the anti-malarial drug pyrimethamine to treat toxoplasmosis in warm-blooded animals. This study explores the research findings and the work behaviours of SN (SMZ and SDZ) drugs. The areas covered include SN drug structure, SN drug antibacterial activity, SN drug toxicity, and SN environmental toxicity.

Keywords Sulfonamide · Sulfamethazine · Sulfadiazine · Toxicology · Environment · Bio-macromolecules

Introduction

Sulfonamides (SN) or sulfanilamides belong to an important class of synthetic antimicrobial drugs that are pharmacologically used as broad spectrum for the treatment of human and animal bacterial infections (Seydel 1968; Supuran et al. 2003). SN structures are organo-sulphur compounds containing the -SO_2NH_2 and/or -SO_2NH- group and are characteristic of the existence of sulfanilamide group and a distinct 6- or 5-membered heterocyclic rings. SNs are not readily biodegradable and have potential to cause various unfavourable side effects including diseases of the digestive and respiratory tracts (Sultan 2015) (with some of the SN drug non-allergic reactions include diarrhoea, nausea, vomiting, dizziness, candidiasis, folate deficiency, and headaches (Mathews et al. 2015)). When used in large doses, SN drugs may cause a strong allergic reaction with two of the most serious being Stevens–Johnson syndrome and toxic epidermal necrolysis (Shah et al. 2018). The overall incidence of adverse drug reactions to sulfanamide allergy is approximately 3–8%, close to that seen for penicillin (Giles et al. 2019; Warrington et al. 2018). A key determinant feature of this allergic response involves substitution at the N4 arylamine group position such as is found in sulfamethoxazole, sulfasalazine and sulfadiazine (Dibbern and Montanaro 2008; Tilles 2001). Other SN drugs which do not contain the arylamine group tend not to induce the allergic response and may therefore be safely taken (Giles et al. 2019; Khan et al. 2019). As a result of this allergy effect, SNs are classified into two groups: (i) anti-bacterial sulfonamides (with an aromatic amine) and (ii) non-antibacterial sulphonamides (without an aromatic amine) (Igwe and Okoro 2014; Yousef et al. 2018; Zawodniak et al. 2010).

SN-derived drugs developed up till the present include sulfamethazine, sulfadiazine, sulfamethoxazole, sulfasalazine, sulfisoxazole, sulfamerazine, sulfadimethoxine, sulfafurazole, and sulphanilamide ("Antibacterial Agents, Sulfonamides" 1944; Hehui et al. 2021; Supuran 2017) (Table 1). Among these SN derivatives, the first to be developed in 1906 was sulphanilamide, although it was not used as an antimicrobial agent until the late 1930s (Ballentine 1981; Fernández-Villa et al. 2019). Sulfamethazine (SMZ) and sulfadiazine (SDZ) are among the derivatives of sulphonamides group of antibiotic drugs that contain the aromatic amine group. SMZ and

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Table 1 Summary of DFT study on SN, SMZ, and SDZ

Sl no.	Molecule/Complex	Method	Basis set	Energy gap/Magnetic moment (μ_{eff})	Year	Reference
1	Sulfonamide in gas and DMSO phase	DFT	B3LYP/6-31G (d, p)	6.10 eV, 6.14 eV	2014	Boufas et al. (2014)
2	Sulfonamide moiety	Geometry optimization	M06-2X/6-311+G (d,p)	0.27 a.u(singlet) 0.21 a.u(triplet)	2018	Ge et al. (2018)
3	Sulfonamide I and II	DFT	B3LYP/6-31G (d, p)	5.38 eV, 5.33 eV	2019	Arshad et al. (2019)
4	Sulfadiazine	DFT	B3LYP/6-31G++(d,p)	-	2009	Ogruc-ildiz et al. (2009)
5	Sulfadiazine	DFT	B3LYP/6-31G (d, p)	4.347 eV	2019	Dubey and Patel (2019)
6	Sulfadiazine Ru(II) and Rh(III) complexes	DFT	B3LYP/6-31G (d, p)	-	2020	Mansour and Radacki (2020)
7	Sulfamethazine Fe(III) complexes (binary and ternary)	TD-DFT	DFT/B3LYP	6.05 μ_B 6.16 μ_B	2014	Mansour (2014)
8	Sulfamethazine Cu(II)	TD-DFT	DFT/B3LYP/LANL2DZ	1.53 μ_B	2015	Mansour and Mohamed (2015)
9	Sulfamethazine	DFT	B3LYP/6-31+G(d,p)	4.979 eV	2015	Won et al. (2015)
10	Sulfamethazine in water	DFT	B3LYP/6-31+G(d)	-	2018	Hazhir et al. (2018b)

SDZ are commonly used in veterinary medicine as an antibacterial compound to treat livestock diseases such as gastrointestinal and respiratory tract infections (Rama et al. 2017). SMZ has been used in animal feeds or feed additives to promote growth in animals (Awaisheh et al. 2019; Burbee et al. 1985; Chattopadhyay 2014; Dixon-Holland 1992). SDZ on the other hand is used primarily on the treatment of infection caused by the burn wounds (Banerjee et al. 2019; Dai et al. 2010; Hosseini et al. 2007). SDZ is also used in combination with the anti-malarial drug pyrimethamine to treat toxoplasmosis in mammals (Hossein Eshghia et al. 2011; Islam et al. 2013; Winters and Janney 2015). There are several reports about SN, SMZ, and SDZ that deal with its environmental effects, antibacterial effects, and its interactions with specific bio-macromolecules (Bendjeddou et al. 2016; Biošić et al. 2017; Chen et al. 2012; Genç et al. 2008a; Islam et al. 2016; Qadir et al. 2015). It is the intention of the present review article to critically assess these reports.

Structure and nomenclature

The typical structure of a tertiary SN involves a central sulfur atom, with two doubly bonded oxygens, that is also bonded to a nitrogen atom (existing as a substituted amine) and an aniline group (Fig. 1a) in which R_1/R_2 may also be hydrogen, alkyl, aryl, or hetero aryl groups. An alternative means of describing the prototypical SN drug structure is an organic compound consisting of aniline derivatized with a sulfonamide group (Pareek et al. 2013; Sonu et al. 2017). The difference in the derivative structure of SN (Fig. 1a) between SMZ and SDZ (Fig. 1 b and c) lies in the extra dimethyl group that is present in the 4th and 6th carbon of the pyridine ring. The IUPAC name of SN is 4-aminobenzenesulfonamide, and the two derivative drugs are 4-amino-N-(4, 6-dimethylpyrimidin-2-yl) benzene sulphonamide for SMZ and 4-amino-N-(pyrimidin-2-yl) benzene-1-sulphonamide for SDZ respectively (Robertson et al. 2020; "Sulfamethazine and Its Sodium Salt" 2001).

Synthetic aspect

There are a number of published methods for the synthesis of sulfonamides in different research papers (Naredla and Klumpp 2013; Shah et al. 2018) yet the most frequent and common method involves a reaction of aliphatic or aromatic sulfonyl chloride with ammonia which produces a greater yield as compared with that of other methods (Bahrami et al. 2009; Dominique Guianvarc'h et al. 2004). The initial compound for the sulphonamide synthesis is benzene which follows six more steps to procure the product. Benzene undergoes nitration to give nitrobenzene which is then reduced by the reducing agent tin and hydrochloric acid to give anilinium ion and is further converted to aniline using sodium hydroxide. Acetanilide produced via acetylation in the aqueous medium then reacts with chlorosulfonic acid to give 4-acetamidobenzenesulfonyl chloride. The intermediate thus formed gives 4-acetamidobenzene sulphonamide in the presence of ammonia. The final step of the synthesis involves hydrolysis in acidic medium to form 4-aminobenzenesulfonamide (sulphanilamide). The schematic representation for the synthesis of sulfonamide drug is shown in Fig. 2 (Tacic et al. 2017). Further derivatives were synthesized using 4-acetamidobenzenesulfonyl chloride with 4,6-dimethylpyrimidin-2-amine (obtained from reacting pentane-2,4-diol with gaunidine) for SMZ (Lu and Rohani 2010; Ross and Plainfield 1968) and pyrimidine-2-amine (obtained from

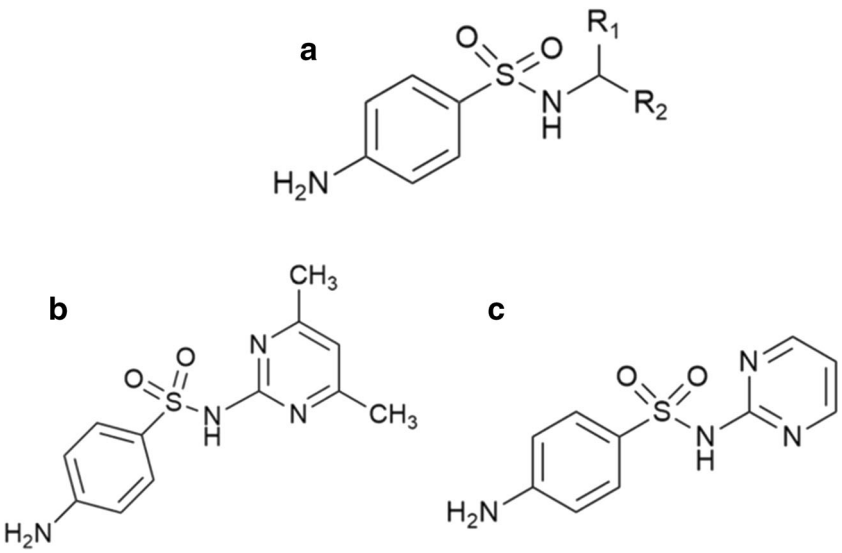

Fig. 1 Chemical structures of **a** a generic tertiary sulfonamide (SN), **b** sulfamethazine (SMZ), and **c** sulfadiazine (SDZ)

reacting malonaldehyde with gaunidine) for SDZ (Donizete et al. 2005; Ma et al. 2015; Shun-ichi Yamada et al. 1950) respectively, as shown in Fig. 3.

Density functional theory study

Density functional theory (DFT) is a computational method that is frequently employed for theoretical simulation of an organic compound's electronic in structure (Karataş et al. 2017; Van Mourik et al. 2014; Verma 2018). The frontier molecular orbital (FMO) analysis is a useful property to determine molecular reactivity and electronic structure, as well as providing information on electronic transitions within molecules (Arshad et al. 2015). The chemical stability of molecules can be explained on the basis of energy gap between electronic transitions of HOMO (highest occupied molecular orbital) and LUMO (lowest unoccupied molecular orbital) (Huang et al. 2017; Mathammal et al. 2013; Xu et al. 2020). A higher HOMO–LUMO energy gap reflects high kinetic stability and low chemical reactivity (stable towards oxidation and reduction reactions) (Farooq et al. 2019; Khan et al. 2018; Rasool et al. 2016). The calculated energy of the HOMO orbital relates to the ionization energy (I. E.), whereas the lower energy LUMO reflects the electron affinity (E. A.) (Ullah et al. 2015). Figures 4 and 5 describe the optimized molecular structure and the electronic transitions (HOMO-LUMO) of the drug SN and its derivatives SMZ and SDZ respectively. Some reports based on DFT simulation of SN, SMZ, and SDZ molecules describing the basis set used and their energy gap difference were reviewed with this information summarized in Table 1. The energy gap gives the relative idea of the stability with the molecule with SMZ being comparatively more stable than that of its parent molecule SN and its fellow derivative SDZ. The observed effective magnetic moment (μ_{eff}) values obtained for SMZ are also in the acceptable range for non-interacting magnetically diluted iron and copper complexes (Kato et al. 1964; Kohout and Krätsmár-Šmogrovič 1968).

Antibacterial activity

Sulphonamides are an important class of antibiotic drugs with a wide range of activity, being very effective against gram-positive and certain gram-negative bacteria (White and Cooper 2003). Some of the susceptible gram-negative bacteria include *Klebsiella*, *Salmonella*, *Escherichia coli*, and *Enterobacter* species; however, sulfonamides show no inhibitory activity (bacterial resistance) against *Pseudomonas aeruginosa* and *Serratia* species.(Lavanya 2017). Sulphonamides are utilized in the treatment of *tonsillitis*, *septicemia*, *meningococcal meningitis*, *bacillary* dysentery, and number of infections of urinary tract (Seneca 2015; Wiedemann et al. 2014). Sulfonamides also show inhibitory activity against some fungi (*Pneumocystis carinii*) and protozoa (*Toxoplasma*, *Coccidia*) (Chio et al. 1996; McFarland et al. 2016). There are many published reports showing antibacterial action by sulphonamide, sulfamethazine, and sulfadiazine drugs (Blanchard et al. 2016; Majewsky et al. 2014; Peng et al. 2015; Reddy et al. 2012; Tailor and Patel 2015; Ueda et al. 2020). SN and its derivatives showed pronounced antimicrobial activity when used against bacterial infections caused by *Nocardia*, *Staphylococcus aureus* and *Escherichia coli* (Genç et al. 2008b; Isik and Özdemir-Kocak 2009a). Increased antibacterial activity of the SN drug group was seen upon substitution with electron withdrawing groups such as the nitro group (Genç et al. 2008a; Isik and Özdemir-Kocak 2009b; Radha Mothilal and Thamaraichelvan 2016; Tailor and Patel 2015; Vagdevi 2018).

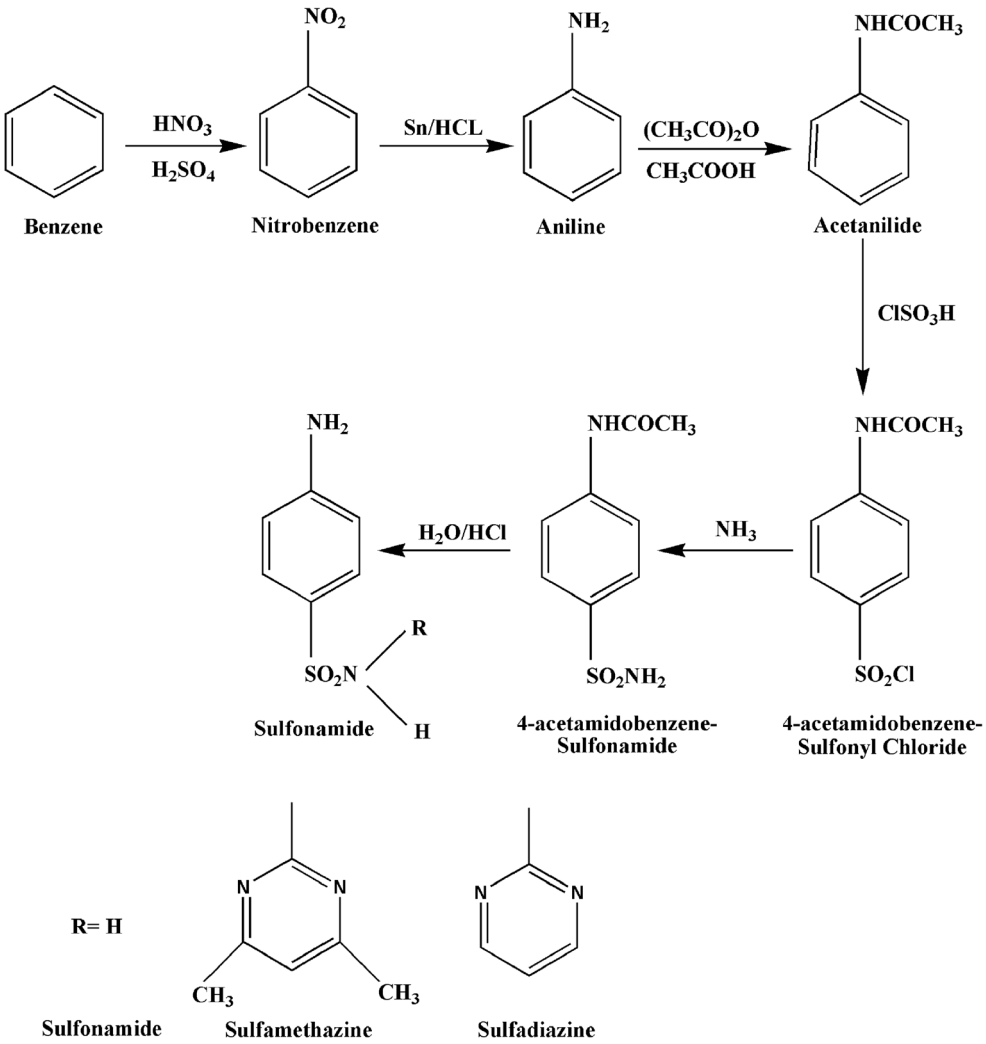

Fig. 2 Schematic representation of the synthesis of sulphonamide in aqueous medium at room temperature (Tacic et al. 2017)

Mechanism and mode of action

Antibiotics are chemotherapeutic agents used to inhibit or kill bacteria. Sulphonamides are competitive antagonists and structural analogues of *p*-aminobenzoic acid (PABA) in the synthesis of folic acid which is essential for the further production of DNA in the bacteria (Zessel et al. 2014). Similarity between the structures (Fig. 5) of SN and PABA allows SN to inhibit and replace PABA in the enzyme dihydropteroate synthetase (whose activity is important for the production of folate) and eventually inhibits the formation of dihydrofolate, tetrahydrofolate and also subsequently inhibits bacterial DNA growth and cell division or replication (Fig. 6) (Pareek et al. 2013). SN drugs along with trimethoprim are used to prevent the synthesis of tetrahydrofolate which further stops DNA replication. The effects of the drug give rise to hindrances in cell division, making the SN drugs bacteriostatic rather than bactericidal (Bohni 1976; Nemeth et al. 2015; Wood and Austrain 1941).

Folic acid (vitamin B9) is essential for the body cell growth and development in humans as it is required for the synthesis, repair, and methylation of DNA (Mahmood 2014). As a consequence, folic acid is critically important for women during pregnancy for a healthy foetus and also for men to improve sperm counts and motility (Dunlap et al. 2011; Gao et al. 2016). Sulfa drugs do not cause disruption in animal cells because they do not synthesize folate, but rather they consume it in the form of dietary requirement, with folic acid performing its functions only after its conversion to tetrahydrofolic acid by dihydrofolate reductase (which is believed to be slow in humans) (Bailey and Ayling 2009). Disturbances in the production of tetrahydrofolate by the SN type drugs can cause abnormality in the DNA by not providing sufficient methyl groups for methylation thereby limiting DNA synthesis which can potentially lead to carcinogenesis (Weinstein et al. 2003) (Fig. 7).

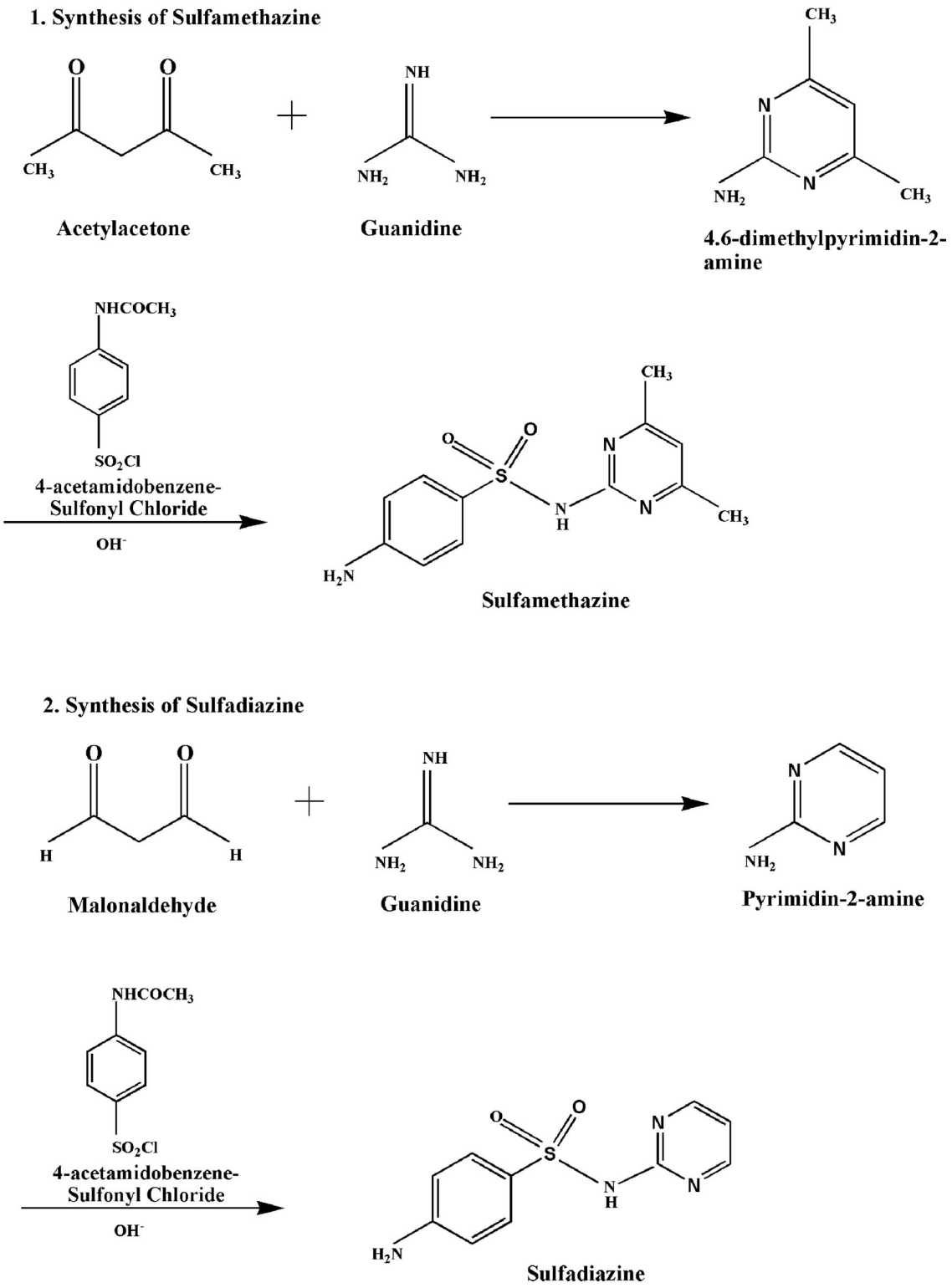

Fig. 3 Schematic representation for the synthesis of sulfamethazine in acetone and pyridine (Banes 1974) and sulfadiazine in acetic acid solution (Abraham 1966; Shun-ichi Yamada et al. 1950)

Bacterial resistance to sulphonamides

Antimicrobial resistance poses an ever increasing threat to mankind, animal, and environmental health (Prestinaci et al. 2015; Taneja and Sharma 2019). A major cause of antimicrobial resistance is the overuse of these medications; another factor is the unavailability and/or lack of new drugs to overcome the problem (Aslam et al. 2018; Ventola 2015). Bacteria

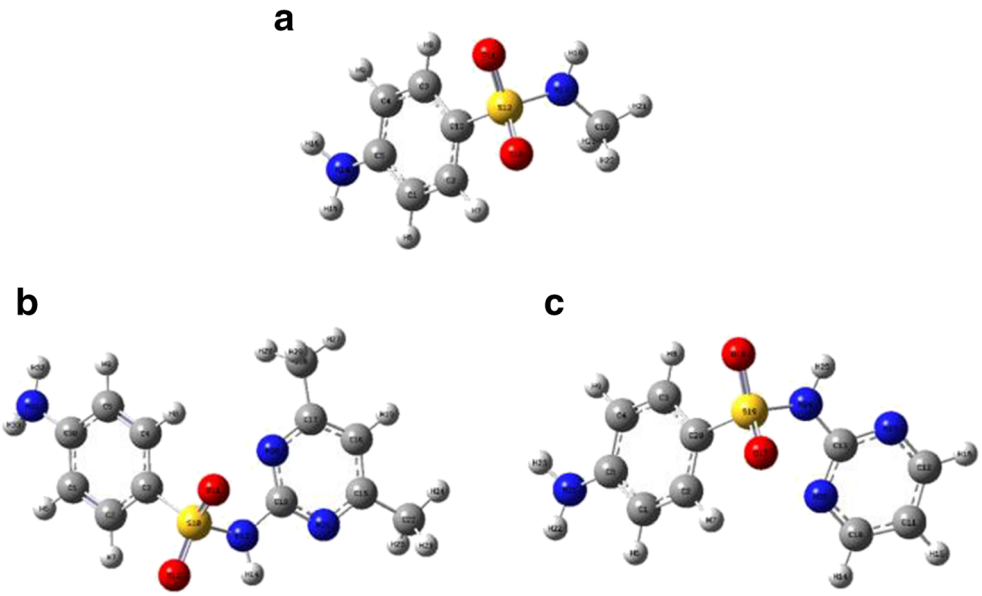

Fig. 4 DFT optimized structure of **a** sulphonamide, **b** sulfamethazine, and **c** sulfadiazine (Arshad et al. 2019; Hazhir et al. 2018a; Huschek et al. 2008).

can resist antibiotic medicines in two different ways—either by endogenous vertical evolution or by exogenous horizontal evolution (Courvalin 2008; Laws et al. 2019). Vertical evolution refers to the gaining of resistance from mutation occurring spontaneously within the bacterial genome that subsequently transfers to its offspring, whereas horizontal evolution describes the transfer of resistance genes between non-related bacteria (Laws et al. 2019). Bacterial resistance to SN has been frequently reported with some of the reported resistance cases being due to (i) resistance bacterial genes to trimethoprim-sulfamethoxazole (used as prophylaxis for the treatment of severe respiratory tract infections) (*Pneumocystis carinii*)(Pentti Huovinen 2001), (ii) resistance genes to SDZ resulted in phenotypic conversion showing a lack of sensitivity to polymyxin B for *Serratia marcescen* (Greenfield and Feingold 2014), (iii) resistance bacterial genes to SN spread and distributed in soils and were detected around poultry farms in China (Wang et al. 2014), (iv) resistance bacterial genes to SN discovered in environment (Razavi et al. 2017), and (v) trimethoprim-SN resistance spread among pathogenic bacteria (Huovinen et al. 1995). With increasing antibiotic resistance to SN drugs, considerable effort needs to be directed to the development of new and effective medicines.

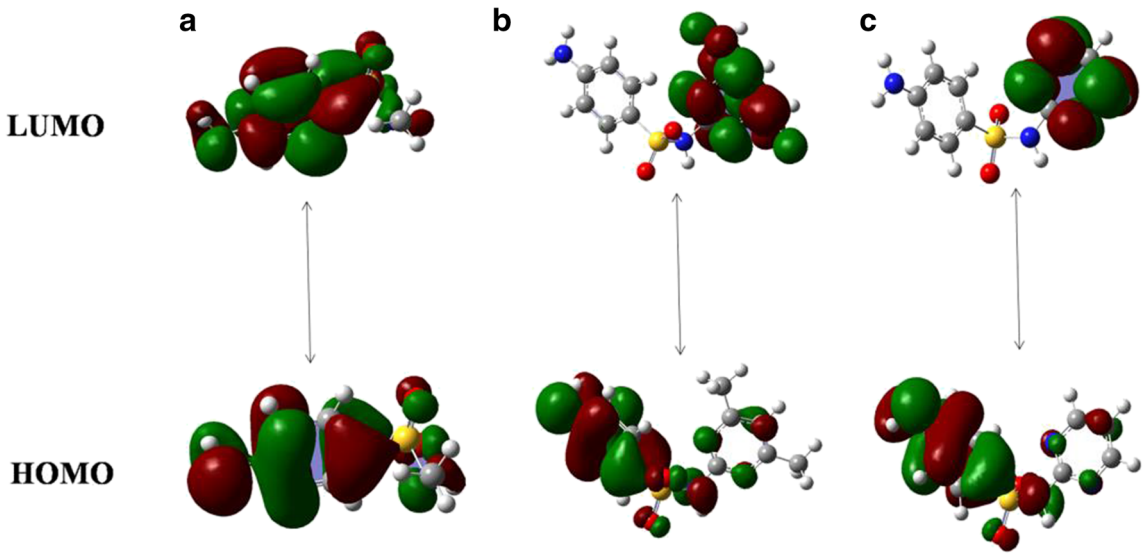

Fig. 5 DFT HOMO-LUMO energy levels of **a** sulphonamide, **b** sulfamethazine, and **c** sulfadiazine (Acar Selçuki et al. 2020; Krawczyk 2015; Mekala and Mathammal 2012).

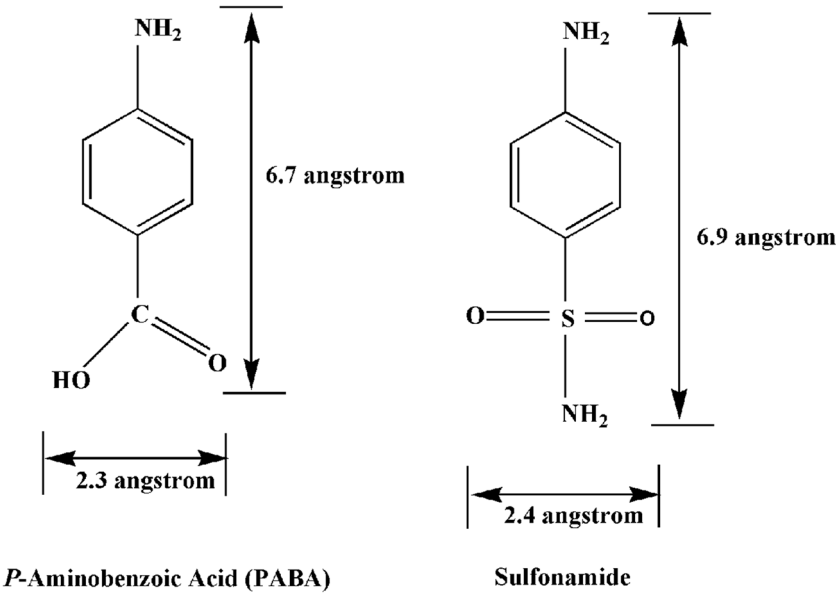

Fig. 6 Structural similarity between PABA and sulphonamide (Tacic et al. 2017)

Environmental effect

The ability of antibiotics to fight against bacterial infections plays an important role in the management of infectious diseases in humans, animals, and microorganisms. However, the overuse and misuse of antibiotics and their release into the environment can potentially pose a threat to animals and microbial communities in soil and aquatic environment (Cycoń et al. 2019; Ding and He 2010; Kraemer et al. 2019). As mentioned, SNs are frequently used antibiotics for animals (e.g. cattle and pigs) and humans for the treatment of bacterial diseases. Both after and during the use of these medicines a high fraction of the drug/medicine is excreted without metabolism through the urine or faeces, with these excretions then released into the environment as manure or sewage (Lin and Tsai 2009). Such observations provide grounds for investigation into SN drugs, covering their detection and distribution in the surrounding environment. SN drugs were also found to exist in low, but detectable levels, in the edible tissues of meat-producing animals treated with SN drugs (Bjurling

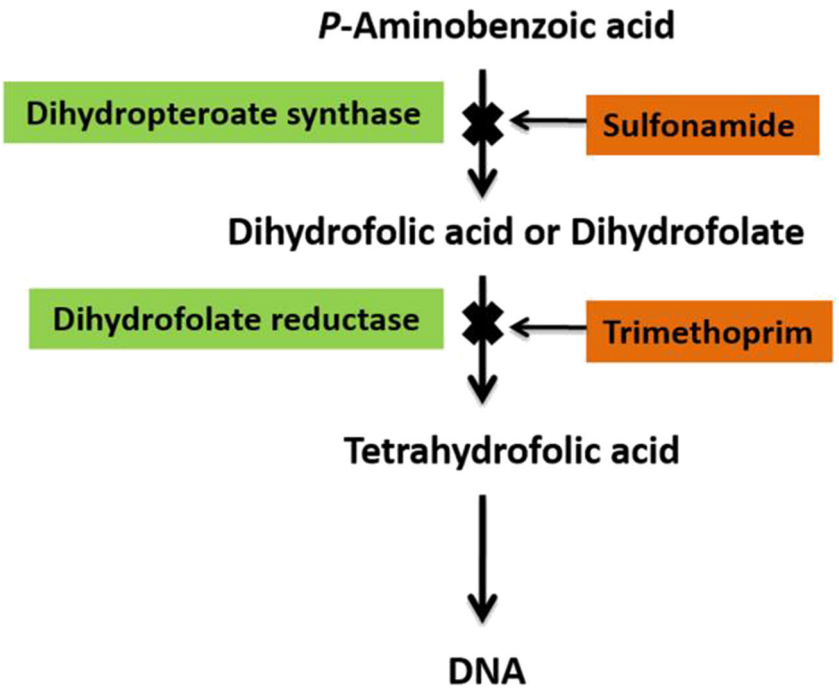

Fig. 7 Synthesis of tetrahydrofolic acid and the mode of sulfonamide action on the synthesis of tertahydrofolic acid (Lavanya 2017; Pareek et al. 2013)

Table 2 Summary on SN-bio-macromolecule binding study

Sl no.	Complex	Technique	Binding constant (M^{-1})	No. of binding sites	Year	Reference
1	Sulfonamide-bovine carbonic anhydrase	Fluorescence spectroscopy	2.5×10^7 (dissociation constant)	-	1967	Chen and Kernohan (1967)
2	Sulfonamide-erythrocyte protein	Michaelis-Menten method	-	-	1989	Matsumoto (1989)
3	Sulfonamides-human carbonic anhydrase I enzyme	Crystallography	-	-	1994	Chakravarty and Kannan (1994)
4	Sulfonamide substituted 8-hydroxyquinoline-DNA	UV-Vis spectroscopy, gel electrophoresis	-	-	2011	Ixit et al. (2011)
5	Sulfonamide-human serum albumin	Isothermal titration calorimetry	2.2×10^6	1	2012	Behbehani et al. (2013)
6	Aryl bis-sulfonamides-enzyme IspF	Mass spectrometry, molecular docking	-	-	2013	Katharina Root et al. (2013)
7	Sulfonamide derivatives- bovine serum albumin	Fluorescence spectroscopy	4.8×10^4 to 1.5×10^5	1	2014	Zhang et al. (2014)
8	Sulfonamides-Ovalbumin	Fluorescence spectroscopy	1.20 to 30.66×10^5	1	2019	Carolina et al. (2019)
9	Cobalt complex sulfonamide-DNA	UV-Vis spectroscopy	1.6×10^5	1	2019	Pandya et al. (2019)

et al. 2000; Hruska and Franek 2012; Poirier et al. 1999). These poorly metabolized antibiotics also accumulate within the soil which can impact soil microbial communities and functions (Thiele-Bruhn and Beck 2005; S. Wang et al. 2021). The sorption of SMZ antibiotics within the soil by black carbon has also been reported as a possible form of bioremediation (Chen et al. 2012). Trace determination of such antibiotics like SMZ and SDZ in animal feeds, human urine, and wastewater (aquatic environment) using different techniques have been variously reported (Blakemore and Thompson 1981; Ji et al. 2012; Mcardell et al. 2004). The environmental behaviour of SMZ and SDZ as reported by Biošić et al. (2017) concluded that their metabolites can bioaccumulate in the aquatic environment if they are not exposed to sunlight (Biošić et al. 2017).

Toxicological effect

Any drug used as medication can cause side effects. Antibiotics are sometime used in a manner which does not provide any benefit and can potentially cause harm (e.g. when used against certain viral infections such as common cold). As such antibiotics are not always the preferred solution as associated toxicological side effects may place the patient in unnecessary hazard. Some of the factors influencing the toxicological effect of SN drugs include duration and dosage of the drug, existence of the heterocyclic ring in N1 substituted SN, its solubility in blood and in other biological fluids, kidney state, age, and nutritional status of patient.(Shmukler et al. 2000) A research report by Boufas et al. (2014) outlined that SNs are somewhat toxic for blood cells, with sulphanilamide

Table 3 Summary on SMZ-bio-macromolecule binding study

Sl no.	Complex	Technique	Binding constant (M^{-1})	No. of binding sites	Year	Reference
1	Sulfamethazine-lysozyme	Fluorescence spectroscopy	-	1	1984	Atef et al. (1984)
2	Sulfamethazine-immunoglobulin G	Purification	10^6 (dissociation constant)	-	2003	Liu et al. (2003)
3	Sulfamethazine- bovine serum albumin	Fluorescence spectroscopy	2×10^6	1	2011	Dawoud Bani-Yaseen (2011)
4	Sulfamethazine- human serum albumin	Fluorescence spectroscopy	1.09×10^4	1.14	2012	Chen et al. (2012)
5	Sulfamethazine-human immunoglobulin G	Fluorescence spectroscopy	2×10^4	1	2015	Wang et al. (2015)
6	Sulfamethazine- bovine serum albumin, adenine	Fluorescence spectroscopy	1.32×10^5 2.11×10^4	0.98 0.92	2015	Rajendiran and Thulasidhasan (2015)
7	Sulfamethazine N-acetylation-human N-acetyltrasferase-2	HPLC	-	-	2015	Tahir et al. (2016)
8	Sulfamethazine-cyclodextrins	Fluorescence spectroscopy	-	-	2019	Ameen and Szente 2019)

Table 4 Summary on SDZ-bio-macromolecule binding study

Sl no.	Complex	Technique	Binding constant (M^{-1})	No. of binding sites	Year	Reference
1	Silver sulfadiazine-DNA	Spectrophotometer	-	-	1972	Rosenkranz (1972)
2	Sulfadiazine-bovine serum albumin	Fluorescence spectroscopy	2.48×10^4	1	2013	Sajid and Hamad (2013)
3	Sulfadiazine sodium-ct-DNA, HSA	Fluorescence spectroscopy	1.06×10^4, 1.63×10^4	1,1	2013	Geng et al. (2013)
4	Sulfadiazine-ct DNA	UV-Vis spectroscopy	2.87×10^3	2	2013	Fotouhi et al. (2013)
5	Sulfadiazine-water-soluble proteins	Fluorescence spectroscopy	10^4-10^5	1	2013	Islam et al. (2013)
6	Sulfadiazine-human serum albumin	Fluorescence spectroscopy	3.90×10^4	1	2014	Ali and Al-lohedan (2014)
7	Sulfadiazine-human serum albumin	Fluorescence spectroscopy	1.28×10^4	0.99	2014	Huang and Liu (2014)
8	Polycation sulfadiazine-DNA	Synthesis, fluorescence spectroscopy	-	-	2015	Long et al. (2015)
9	Sulfadiazine-ureases	Synthesis, molecular docking	-	-	2017	Bean et al. (2017)
10	Sulfadiazine-lysozyme	Fluorescence spectroscopy	1.75×10^4	1	2018	Sonu et al. (2018)

derivative being more toxic comparatively among the SN group of drugs while sulfadiazine was reported the least harmful. SN drugs can produce serious acute haemolytic anaemia (destruction of the red cells) causing agranulocytosis which is capable of depressing blood platelets (Kracke 1944). The potential for toxicity of SMZ in the environment is extant especially when occurring near to water (De Liguoro et al. 2009; Liu et al. 2019; Wood et al. 1957). Toxicity tests in animals of SDZ suggested that it is less toxic in comparison with other SNs while still being highly effective against common pathogens and as such has been exploited for the treatment of human bacterial infections (Finland et al. 1941; Kouroumkis et al. 1974). The measured toxicity of SDZ in water and water bodies suggested a possible increase in its toxic antimicrobial effects following its pH dependent chemical degradation, with a decrease in toxicity at higher pH values (Liu et al. 2016; Taylor et al. 2014).

Bio-macromolecule binding interaction study

SN type drugs, such as SMZ and SDZ, are widely used antibiotics with a plethora of drug targets (Islam et al. 2013; Lv et al. 2013; Sajid and Hamad 2013; Uhlemann et al. 2021). The study of which bio-macromolecules these drugs show affinity for helps us to understand their effect on humans, animals, and microorganisms. Tables 2, 3, and 4 summarize SN, SMZ, and SDZ interaction studies with a range of bio-macromolecules. The nature of the binding is principally described using the parameters of binding affinity and number of binding sites (with the target bio-macromolecule shown in the left hand column). Strong drug binding affinity to the target of $> 10^6\ M^{-1}$ can result in inhibition however the opposite can be expected for weak interaction with the target (binding affinities $< 10^4\ M^{-1}$).

Conclusion

SNs are widely used synthetic antimicrobial drugs due to the fact that they that can be used for diverse purposes (such as treating bacterial infections and also promoting livestock growth). There are various forms of SN drug derivatives that have been produced of which SMZ and SDZ are the most frequently used. The purpose of this review was to examine SN drug structure, function, and toxicity in treated human and animal patients as well as the environment. This study has made clear the drug mode of action in its inhibition of bacteria through its competitive inhibition of bacterial DNA synthesis. The nomenclature and structure of the drugs (at the DFT level of approximation) have been discussed. Literature of its toxicological effect upon the environment, animals and human beings has also been reviewed.

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