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Review the Antibacterial Activity of Sulfonamides Derivatives

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Abstract : It is now clinically necessary to develop new classes of antibiotic medicines due to the growth in medication resistance. Worldwide, there is still a great demand for the creation of antibacterial agents with new modes of action. antibiotics for bacterial infectionsremains a challenge given the emergence of incurable diseases and the riseinmicrobiological infections with multiple drug resistance. Consequently, the demand for forceful actions exists.it is essential to identify innovative synthetic analogs and to come up with new, effective therapeutic medicines.in opposition to bacterial objectives. The advantages of new, less damaging, less intrusive technologies,hot research areas in include exceptionally dynamic sulfonyl or sulfonamide-bearing analogs.pharmaceutical chemistry The latest review of sulfonyl developments is presented.or compounds based on sulfonamides that may have antibacterial properties against differentbacterial strains that are Gram-positive and Gram-negative, as well as addressing its many characteristicsRelation between structure and activity (SAR).

Keywords: Sulfonamides ; SAR ; Antibacterial Activities ; Pathogens.

1. Introduction :

The world of medical sciences has undergone a revolution thanks to sulfa medicines that contain the biologically active sulfonamide functional group [1]. Sulfonamides inhibit folic acid, an essential chemical in the production of bacterial DNA and RNA; a deficiency in tetrahydrofolate limits the production of new DNA and RNA, leading to the death of the bacterium. Normal microbial growth is hindered due to bacteria's effort to convert sulfonamide instead of p-amino benzoic acid for the production of folic acid. In agriculture, sulfonamides are useful for fighting bacteria because of their broad spectrum of activity. Medicines containing sulfonamide functional groups have been demonstrated to block carbonic anhydrases, and these carbonic anhydrase inhibitors have showed promise as diuretics, antiobesity medicines, and cancer treatments. In human medicine, sulfonamides are often used, especially for individuals who have reactions to more common antibiotics. animal health care [2]. Due to their antifungal and herbicidal] characteristics, numerous derivatives of sulfonamide have been described for use in agriculture. A growing need for innovative antibacterial medications with distinct modes of action and mechanisms has emerged in order to combat germs that are resistant to currently available medications. After being exposed to or receiving therapeutic treatment with conventional antibiotic drug molecules, harmful organisms (bacteria, fungi, and mold) become significantly more resistant when new species evolve as a consequence of mutation, conjugation, transduction, or transformation. More so than other synthetic procedures, the synthesis of new sulfonamides has caught the attention of researchers because of its history of success in the disciplines of pharmaceutical sciences and medicinal chemistry. A total of ten new sulfonamides were synthesized and characterized in recent studies by reacting p-toluene sulphonyl chloride with

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essential amino acids (histidine and tryptophan) and medications that contain amino groups, such as levetiracetam (anticonvulsant), famotidine (antiulcer), celecoxib (nonsteroidal anti-inflammatory drug), ribavirin (antiviral), tran (vitamin B) [3] and the antimicrobial activity was evaluated Three separate studies' mean standard deviations were used to calculate the inhibitory zone. existed between. After the compounds were synthesized, their antibacterial effects against gram (+) and gram (-) bacteria were evaluated.Bacterial resistance continues to be a worldwide problem despite the introduction and advancement of a few antibiotic classes over the last 100 years. There are a few solutions available right now [1]. Although it is possible to think of bacterial resistance as a natural process, the widespread use—and in many cases abuse—of antibacterial agents in domestic animal farming has led to a false perception of an increase in safe strains, increasing the likelihood that antibacterial resistance microorganisms will eventually contaminate humans [2]. In the past, microbe-caused illnesses have caused an overall high rate of mortality throughout the world. Fortunately, since penicillin's discovery as a powerful antibacterial agent in the 1940s, a variety of natural and man-made antibiotics have significantly improved human health [3]. Due to the emergence of irresistible infections and the rise of multidrug-resistant microbial strains, treating bacterial infections remains difficult. The development of both new and ancient opponents of bacterial resistant bacterial strains in previous decades stimulates a broad necessity for new classes of antibacterial agents, despite the wide range of antibacterial specialists and chemotherapeutics on the market [4–13].

In the settings of an emergency room and the general population, the occurrence of multidrug-resistant (MDR) bacteria results in a severe clinical catastrophe [14]. penicillin-resistant MRSA The main causes of concern are vancomycin-resistant enterococci (VRE) and streptococcus pneumoniae (PRSP). Additionally, this may result from the habitual use of antibiotics to treat non-bacterial infections and from inadequate comfort with the regulatory framework for medication use. In this situation, it is very important for the novel medicinal molecule to be launched as an antibiotic for the treatment of MDR MRSA [15,16]. MRSA is an entrepreneurial microorganism that is often discovered in nosocomial disorders that may result in severe infections, despite the fact that it is present in the human skin florathen in especially the nasal mucosaa [17]. Numerous attempts to develop aformore substantial analog as coresplatform with engineered fitted in a combinatoriall approaches have been undertaken in the preceding decades in the field of medicinal chemistry. Although the large approaches have been successful, between 1962 and 2000 no newest noteworthy class of antibiotics was develop [18].Consequently, there is a pressing need for vigorous efforts to come up with novel active therapeutic drugs. For the microbial target to be tested for medicinal chemistry, it is required to identify new synthetic analogs [19,20]. Despite having strong inhibitory effect against a particular target, single-targeted medicines aren't enticing to biological systems, according to typical clinical encounters [21,22]. The sulfonamide or sulfonyl functional groups have been important subjects in medicinal chemistry [23] since since the first sulfonamide-containing antibacterial drugs were published. Sulfonyl and sulfonamide groups form a large family of drugs that are widely employed as agricultural and pharmacological agents [24,25]. Antibacterial, antifungal, antiinflammatory, antioxidant, diuretic, anticancer, and carbonic anhydrase properties among many others have piqued the attention of biologists and medical professionals in sulfonamides in recent years. Antitumor and GSK inhibitors, amyloidosis, TB, diabetes, HIV/AIDS, malaria, and other diseases that are caused by bacteria have long been treated using sulfonamides. Sulfasalazine, meloxicam, piroxicam, celecoxib, and more than 150 more

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drugs containing Sulfur (SVI) are available on the market with FDA clearance. SVI's varying Pharmacological activity in basic particles determines the most advantageous method for consolidationvia the hybrid strategy, whereby many of the necessary medications are available in Fig. 1: The market .Antibiotics belonging to the monobactam class are betalactams that impede cell wall synthesis in gram-negative bacteria.Antibiotics known as monobactams belong to the -lactam family.monocyclic, and the microorganisms that make it[26]. Unlike the majority of No further rings are connected to the -lactam ring. Monobactams are effective exclusively against aerobic Gram-negative microorganisms (e.g., Neisseria, Pseudomonas) (e.g., Neisseria, Pseudomonas). Monobactams coupled with a siderophore show promise for treating MDR bacteria. An accessible monobactam antibiotic is called aztreonam.Other examples of monobactams are tigemonam, nocardicin A, and tabtoxin. Monobactams have been associated with a variety of potential side effects, including rashes on the skin and, rarely, liver disease that seems out of the ordinary.Drugs containing sulfonamide that having receive FDA approval are offer for sale in pharmacy as shown in a figure No 1[27].

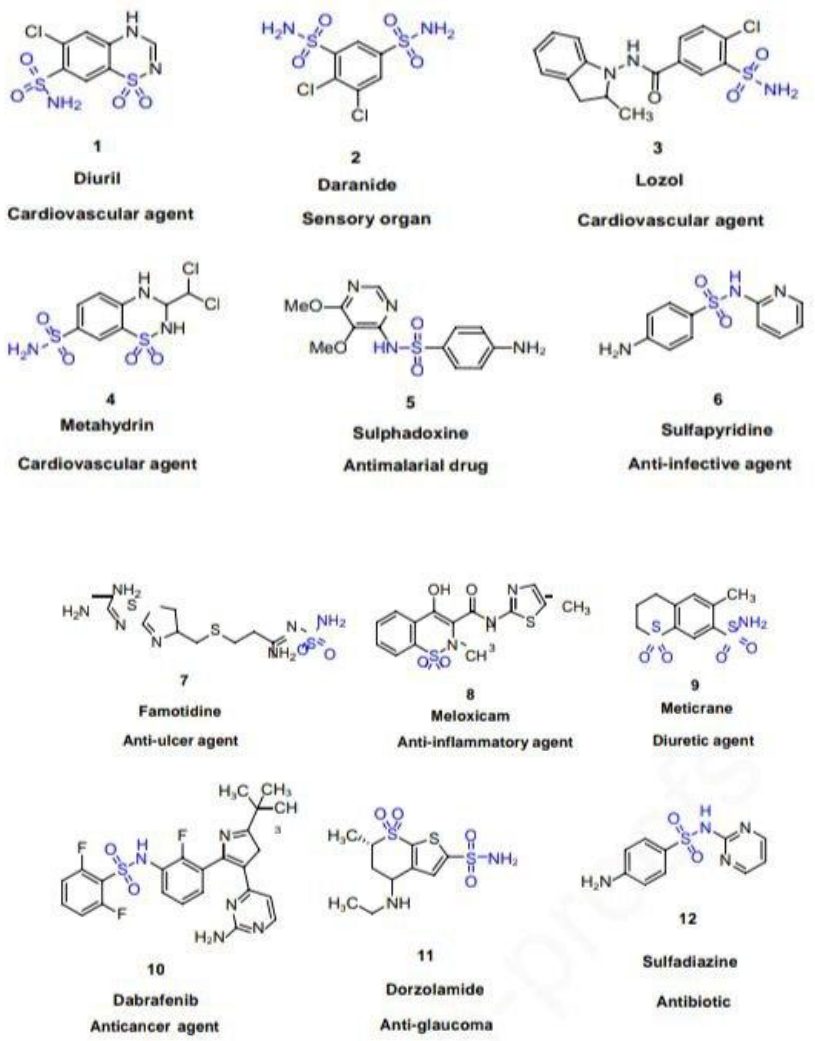

Fig. 1: Drugs containing sulfonamide that having receiveFDA approval are offer for sale in pharmacy.

2. Antibacterial activitiesof sulfonamides containgheterocycles ringcompounds :

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The discovery of penicillin by Alexander Fleming in 1929 and the introduction of the first sulpha drugs by Domagk in 1932 marked a significant increase in the number of novel antimicrobials that were available between 1940 and 1960. Because infectious illnesses could be well-managed and halted thanks to "the time of antibiotics," humanity felt sure that modern medicine would prevail until the early 1970s. However, infections continue to be the second leading cause of mortality globally, accounting for more than 13 million fatalities annually. This situation is the result of the emergence of new illnesses, the resurgence of previously established diseases, and, particularly, the development of antibiotic resistance. In the past, antibiotics were chemicals produced by different types of microorganisms that inhibit the development of other microorganisms and may even lead to their final annihilation. The word "antibiotic" has been expanded in current use to cover both naturally occurring antibiotics that have undergone chemical modification and completely artificial compounds, which are more properly referred to as semi- or synthetic antimicrobial agents. Based on their specificity of goal, antibiotics may be classed as antimicrobials . Broad-spectrum antibiotics are effective against a large variety of microorganisms, whereas "limited-spectrum" antibiotics only affect certain types of bacteria, including gram-positive or gram-negative ones. To treat infectious diseases, contemporary science and technology have contributed much, with the creation of antibiotics being one of the most notable and fruitful examples.However, the spread of antibiotic resistance among bacterial strains and its increasing presence diminished the Chloramphenicol and penicillin are two examples of bacteriostatic and bactericidal antimicrobial mediators, respectively. Efficacy of therapy for a large number of drugs using bactericidal agents. cause the death of bacterial cells, and bacteriostatic drugs prevent the germs from proliferating [28]. Because of the widespread success of antibiotics containing sulfonamides, the sulfonamide beneficial functional group has played a vital role in medicinal chemistry as scientists look for further effective antibacterial agents[29]. Various sulfonyl or sulfonamide containing heterocycles have been used, to date, for For instance, benzimidazole, thiazole, quinazolinones, oxazoles, and pyridazine have all beenefficiently developed and used in sulfadiazine-containing facilities,good antibacterial properties include sulfachlorpyridazine, sulfathiazole, and sulfisoxazole.activity against bacterial strains of both Gram-positive and Gram-negative types, as well as MDRstrains of bacteria . owing to the inadequate effectiveness and even loss of resistance of conventional antibioticsurgent solutions were needed to protect against emerging and novel bacterial pathogens.predicted to create new, much more effective antibacterial drugs that are also less harmful [30].Indicates heterocyclic containing sulfonamides, which may be active as antibacterial as shown in a figure No 2

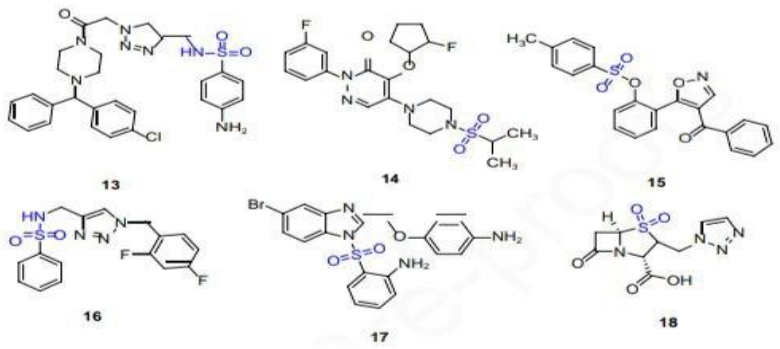

Fig. 2: Indicates heterocyclic containing sulfonamides, which may be active as antibacterial.

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3.Pathogenic bacteria:

The pathogenesis of a bacterial infection includes both the beginning of the infectious process and the processes that ultimately result in the emergence of disease symptoms. Pathogenic bacteria are characterized by their ability to spread, to attach to host cells, and to invade host cells and tissues. Power to poison and escape the host's immune system.Common pathogen-causing bacteria often cause infections with no outward signs of illness. In order for disease to develop, either the germs themselves or the immune system's response to them must do enough damage to the host[31].

3.1. The Staphylococcus genus :

Staphylococcus is a genus of Gram-positive bacterium that are 0.5-1.5 m in size and are distinguished by cocci that split in more than one plane to produce grape-like clusters. These bacteria, which are facultative anaerobes but do not produce spores, have a complicated dietary need for growth[32,33], a low G+C content in their DNA, and are not motile. Staphylococcus is a genus of Gram-positive bacteria that are 0.5-1.5 m in size and are distinguished by cocci that split in more than one plane to produce grape-like clusters.These bacteria are not motiled and do not produce spores; instead, they are facultative anaerobes that have a low G+C content of DNA, can tolerate high salt concentrations, and are resistant to heat. The most dangerous strain of S. aureus[34,35], Staphylococcus, which has been linked to both nosocomial and community-acquired illnesses. In many cases, it colonizes the skin without causing any noticeable symptoms. healthy people's mucous membranes, especially the front nares. It has been calculated that between 20% and 30% of thepopulation are infected with this bacteria permanently, whereas the remaining 30% are only temporarily Carriers make up % of the population, but only temporarily.[36] There is a higher chance of harm because of this colonization. of infection by serving as a source for the spread of germs.while the defenses of the host are down. Since S.aureus plays such a crucial role,diseases, and the spread of antibiotic-resistant bacteria, thisbacteria is now the most well investigated member of the staphylococcal genus [37].

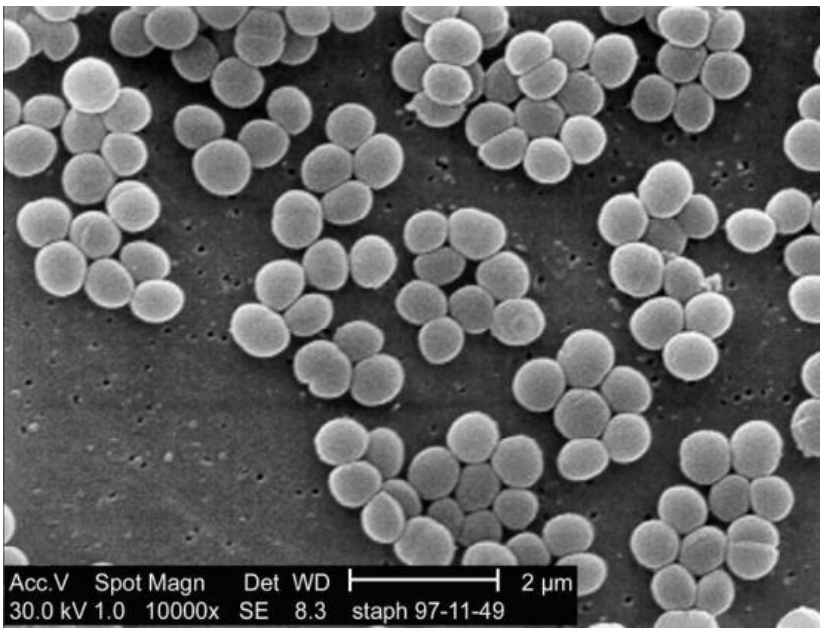

Fig 3 : Imaging Staphylococcus aureus using a Scanning Electron Microscope.

S.aureus is a prominent nosocomial pathogen and is also a clinically important classical pathogen

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responsible for a wide variety of illnesses in the general population. S. aureus-related illnesses may be broken down into the following groups.Food poisoning , scald skin syndrome , and toxic shock syndrome are examples of disorders mediated by toxins (TSS),furuncles, boils, cellulitis, and impetigo are examples of skin and soft tissue infections,infected organs located deep inside the body, such as the bone, joints, heart valves, spleen, and liver ,Pneumonia and catheter-associated urinary tract infection (UTI) are two types of infections that may affect the respiratory and urinary systems.

3.2. Pseudomonasaeruginosa :

The non-fermentative, aerobic Gram-negative rod Pseudomonas aerugionosa (P.aruginosa) ranges in size from 0.5 to 0.8 m to 1.5 to 3.0 m in length and width, respectively. The majority of strains only have one polar flagellum that they use to move about. It has an unusual capacity to colonize ecological niches where resources are scarce, from water and also soil to plant and animals tissues, since it thrives in wet settings and can utilise a broad spectrum of organic molecules for growth.

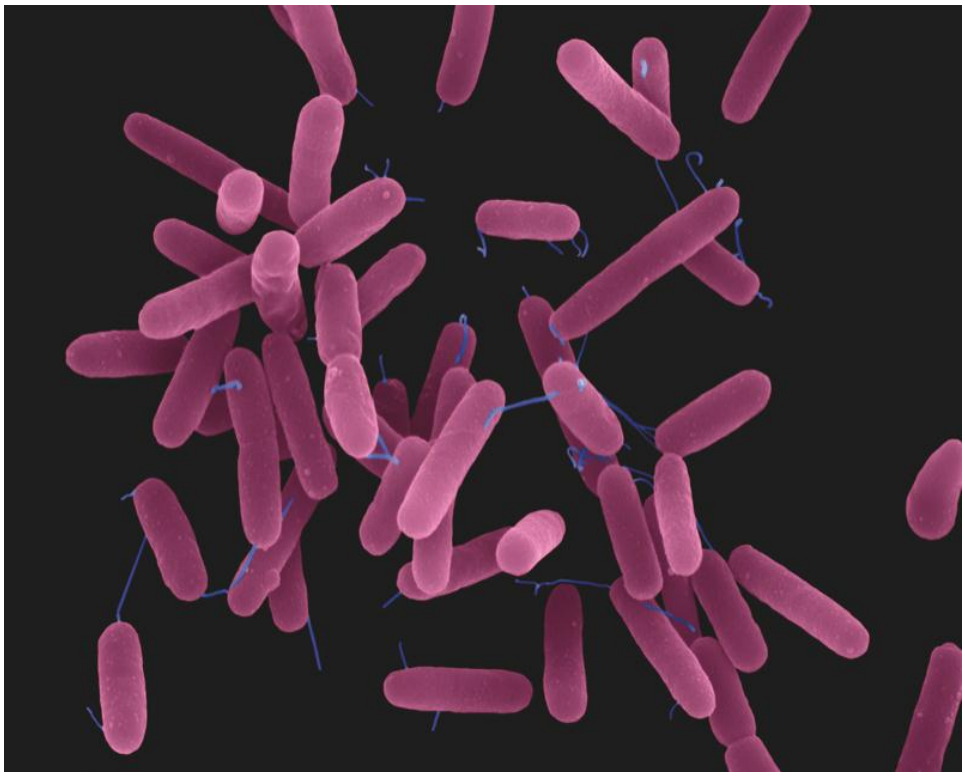

Fig 4 : Pseudomonasaeruginosa

Positive oxidase test, growth at 42 °C, hydrolysis of arginine and gelatine, and nitrate reduction are typical biochemical characteristics of P. aeruginosa isolates. Both pyoverdin and pyocyanin are soluble pigments produced by P.aeruginosa strains. In addition to chronic CF lung infection, Pseudomonas aeruginosa has been linked to a wide range of other infections seen in clinical practice, such as acute septicemia following a burn or surgical wound infection, urinary tract infection, corneal ulceration (due to contact lens wear), endocarditis (due to intravenous drug use, etc.), and pneumonia (due to ventilator and endotracheal tube use) [38]

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4. Mechanisms ofaction ofantibacterial agents :
The following are not considered antimicrobials because of the way they kill bacteria:

A. Interfering with the cytoplasmic membrane :
These drugs (Polymyxins, Daptomycin) are able to enter the cytoplasm of sensitive cells by diffusion via their outer membrane and cell wall. They associate with the cytoplasmic membrane, which they then destabilize and disturb. Ultimately, this results in cell death due to cytoplasm leakage (they are bacteriocidal)[39].

B. Interference with nucleic acid synthesis is caused by two classes of drugs :
Nalidixic acid, ciprofloxacin, levofloxacin, and gemifloxacin are all examples of fluoroquinolones that inhibit the enzyme DNA gyrase and hence prevent DNA synthesis from occurring. After binding to the DNA gyrase-DNA complex, fluoroquinolones release the shattered DNA molecules into the cytoplasm, where they might trigger cell death. Rifampin causes cell death by binding to DNA-dependent RNA polymerase and stopping RNA synthesis (they are bacteriocidal).

C. Interfering with cell wall synthesis :
The -Lactams, which include carbapenems, monobactams, penicillins, and cephalosporins, and the glycopeptides, which include vancomycin and teicoplanin, are not included in this group since they work by inhibiting the production of bacterial cell walls. By interfering with enzymes required to create the peptidoglycan coat, -lactams mediators reduce development of the bacterial cell wall. When glycopeptides bind to the terminal D-alanine residues of nascent peptidoglycan series, they prevent the cell wall from reaching its cross-linking stages, which are necessary for the formation of a solid cell wall (they are bacteriocidal).

D. Reserve of a metabolic pathway :
Folic acid production is impeded by sulfonamides and trimethoprim, which in turn slows down DNA synthesis. Trimethoprim, (a folic acid analogue), and more sulfamethoxazol (asulfonamide), a typical antibacterial medicine combination, inhibits two stages in the enzymatic pathway for the formation of folate in bacteria (they are bacterioststic).

E. Inhibition ofprotein synthesis :
The unique antibacterial properties of chloramphenicol, tetracyclines, aminoglycosides, macrolides, and oxazolidinones are the result of their ability to suppress protein synthesis. Ribosomes in bacteria and eukaryotic cells have different shapes and arrangements. The antibacterial mediators use these differences to inhibit bacterial growth in a targeted manner. Chloramphenicol, in contrast to aminoglycosides, tetracyclines, and macrolides, binds to the 50S subunit of the ribosome (they are bacterioststic). all above mechanism showed in a figure No 5 [40].

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Fig 5: Mechanism of antimicrobial action

5. Methodologies of sulfonamideschemical preparation :

5.1 : Sulfonamides via sulfonyl chloride from thiols :

In light of sulfonamides' versatile nature, it is important to discover efficient and universal strategies for their production. This means there is a consistent need for the production of these chemicals. In the past, various synthesized approaches have been documented. Sulfonyl chloride, transition metals as catalysts, and Grignard reagents are only a few examples of the most popular and cutting-edge approaches.

To make sulfonamides, chlorides are usually sulfonylated with amines in the presence of a base. In the presence of a base, sulfonyl chlorides are subjected to a nucleophilic attack by ammonia, primary or secondary amines. While effective, this technique necessitates the use of sulfonyl chloride, which may be difficult to store and manage. From there, sulfonyl chlorides may be made by bubbling Cl2 gas into an aqueous acid or a biphasic mixture that already contains the thiol. The chlorinating agents SOCl2 [POCl3 , and PCl5 are used to convert sulfonic acids into sulfonyl chlorides. Bahrami et al. recently described the direct oxidative conversion of thiols into sulfonamides using H2O2-SOCl2 (Fig. 6), where upon interaction with amines, the corresponding sulfonamides were formed in good yields in extremely short reaction times[41].

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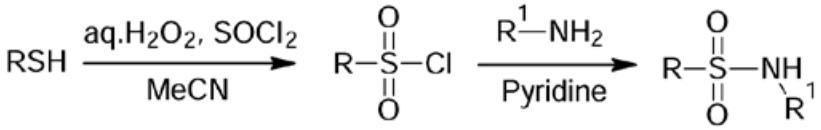

Fig 6 . Conversion of thiols into sulfonamides withing H2O2-SOCl2

The aforementioned strategy was enhanced by reimagining it as a combinatorial library (parallel format). For aryl thiols with either electron-donating or electron-withdrawing substituents, sulfonamides were easily produced in excellent to high yields [28]. Sulfonyl chloride in acetonitrile has recently been modified utilizing N-chlorosuccinimide (NCS) and a tetrabutylammonium chloride-water system. Sulfonylazides may be prepared from thiols in the presence of NaN3 using a one-pot procedure that the authors have described. Jong et al.described a straightforward, one-pot synthesis of sulfonylazides from sulfonic acids.The benefits include strong chemoselectivity, quick response times, low material costs, and straightforward workup (Fig. 7) [42].

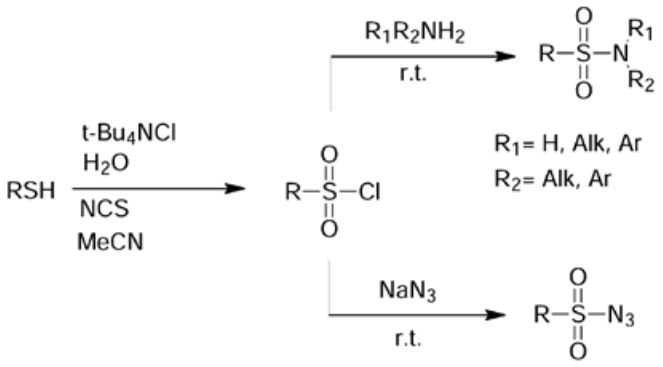

Fig 7.Method concerns the using *N*-chlorosuccinimide (NCS) and *t*-Bu4NCl

Wright et al. described a procedure for the synthesis of sulfonamides from thiols, which involves the oxidation of the thiol with sodium hypochlorite (common bleach) in situ. The use of a manageable quantity of oxidant and easily available reagents are only two of the many benefits of this approach. A further treatment of the resultant sulfonyl chlorides with benzylamine yielded sulfonamides in yields as high as 98%. (Fig 8)[43].

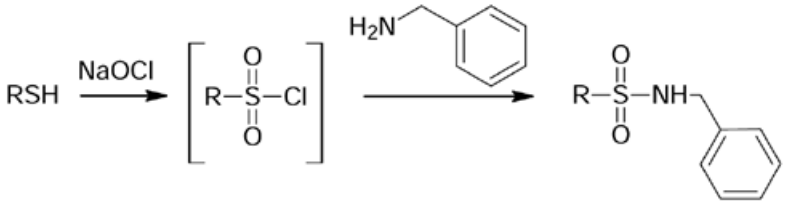

Fig 8 Sodium hypochlorite as mediated oxidation of thiols

A measured quantity of chlorine was synthesized into an aprotic solvent using trichlorocyanuric

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acid (TCCA) and benzyltrimethyl ammonium chloride in water (MeCN). Bonk et al. [44] introduce the usage of TCCA, which has the benefit of producing very pure chlorine in comparison to hypochlorite. The study team improved upon this technique by including the following amine into a one-pot reaction, thereby enabling the production of sulfonyl chloride in situ and the provision of sulfonamides in less than 1 hour (Fig. 9).

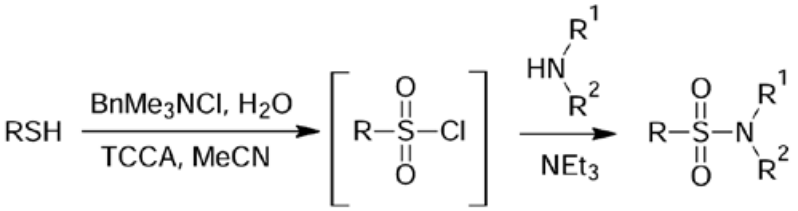

Fig 9. Synthesis of sulfonamides by reaction with trichlorocyanuric acides (TCCA)

5.2 Sulfonamides from sulfonic acid

After sulfonic acid, sulfonyl chloride is a natural byproduct.

This synthesis is done in the microwave and has shown to be practical and efficient due to its high yield and great tolerance for functional groups [45]. (Fig. 10).

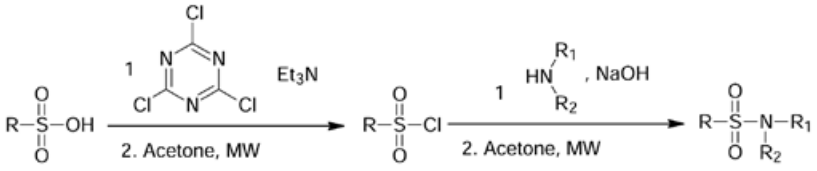

Fig. 10. Synthesis of sulfonamidess with uses microwave irradiation

Excellent to good yields of the appropriate sulfonamide were obtained when this reaction was carried out using traditional heating [46].The unique use of trichloroacetonitriletriphenylphosphine complex (Cl3CCN/PPh3) in sulfonamide synthesis was described by Chavasir et al. Yields are not repeatable when using other solvents or different ratios of Cl3CCN to PPh3 to sulfonic acid, but they are when using dichloromethane and reaching the optimum yield.Not only may heterocyclic and aliphatic sulfonyl chlorides be synthesized using this approach, but also aromatic sulfonyl chlorides, which is a significant benefit (Fig. 11).

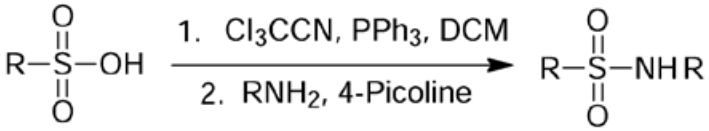

Fig. 11. Method performewith trichloroacetonitril etriphenylphosphine complexes

Also, Barrett et al. showed that sulfur dioxide reacts with a variety of organometallic reagents to

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produce sulfinic acid salts, which may then be directly treated with sulfuryl chloride and amine to generate sulfonamides in high yields. When DABCO and sulfur dioxide are mixed together, a colorless solid chargetransfer complex is produced that may be employed in lieu of gaseous SO2 in organic synthesis; this modification was exploited by Woolven et al. [47].
Sulfinates are produced during Grignard reagent reactions, and they may be transformed on-site to sulfonamides (Fig. 12).

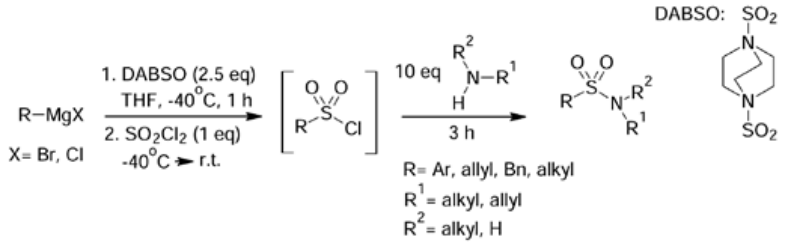

Fig. 12. Synthesis of sulfonamides with usingingorganometallic reagents

5.4Sulfonamides from sulfonamides

The synthesis of 2-amino-9-hydroxypurin-6-sulfonamide is another novel example of a sulfonamides synthesis. Revankar et al.utilized mild and selective oxidants. One equivalent of m-CPBA was used in their report of oxidizing 2-amino-9H-purin-6-sulfenamide, and the resulting yield was 48%. (Fig. 13). An increase in m-CPBA dosage (from 2eq to 4eq) resulted in a marginal improvement in yield (from 47% to 53%) of the active molecule [48].

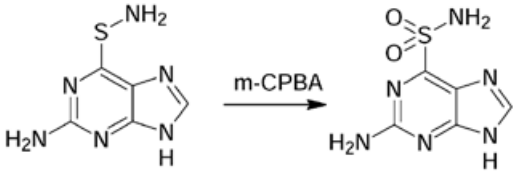

Fig. 13. Oxidation of sulfenamides with using *m*-CPBA

5.5 **Sulfonamides via using transition metal catalyst**

The creation of cross-coupled C-N bonds using transition metal catalysts has been the subject of much research, with the Buchwald-Hartwig reaction being the most well-known example of a N-arylation using a palladium catalyst. For N-arylation of sulfonamides, only a small number of transition metal-based catalysts have been investigated so far. Here we have Pd, the first. For a Pd-catalyzed sulfonamidation of aryl nonafluorobutanesulfonates, the best base-solvent combination was determined to be t-BuXPhos and K3PO4 in tert-amyl alcohol. Different types of functional groups were tolerated by the reaction conditions.The ineffective participation of 2,6-disubstituted aryl nonaflates in the reaction has been recognized as the sole restriction of this approach [49]. (Fig. 14).

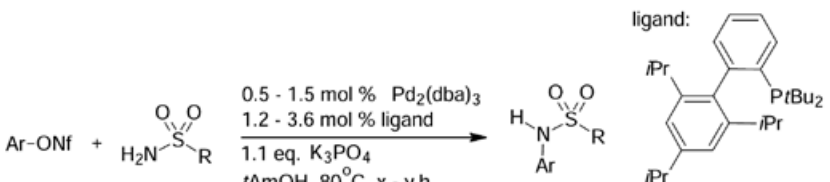

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Fig. 14. Pd-catalyzed sulfonamidation

6. Conclusion:

Microbes with multidrug resistance, such as Gram-positive and Gram-negative bacteria and certain tumors, pose a serious threat to patient health in hospital and community settings. Consequently, we need fresh professionals in the field of antibacterials with unique techniques of actionare urgently required, and research on these substances has already begun. As of right now, thereview focused on the cutting edge of medicinal chemistry in the quest for novel synthetic structures to test as potential antibacterial medicines; SAR investigations of these compounds were also included. considered with the purpose of advancing the logical development of such derivatives. An appropriate replacement comprising electrondonating/accepting atoms was selected based on SAR of expressed derivatives.withholding groups that include heterocyclic moieties linked to sulfonyl orIn modifying antibacterial activity, the sulfonamide-skeleton plays a crucial role.
References show that the author, Bassam A. Hasan, was responsible for the development of a number of heterocyclic compounds and active plant ingredients with major medicinal efficacy, such as menthion [50-57].

7. references :

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