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(REVIEW ARTICLE)

A review of compounds derivatives with antimicrobial activities

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Abstract

Antimicrobial resistance represents a serious threat to human health across the globe. The cost of bringing a new antibiotic from discovery to market is high and return on investment is low. Furthermore, the development of new antibiotics has slowed dramatically since the 1950s' golden age of discovery. Medicinal compounds synthesis produce a variety of bioactive compounds that could be used to build a new way for the future discovery pipeline. While many studies have focused on specific aspects of synthetic compounds with antibacterial properties, a comprehensive review of the antibacterial potential of compounds has never before been attempted. This review aims to evaluate reports on some derivatives with significant antimicrobial activities.

Keywords: Antimicrobial activities; Medicinal compounds; Synthetic derivatives; Heterocyclic compounds

1. Introduction

Chemical compounds in a remarkably important section in the present world and group of different applications in various fields. Thus, continuously research work has been carried out for the synthesis of new chemical compounds counting synthesis of derivatives of naturally finding ones. Heterocycles mainly containing heteroatom nitrogen and sulfur have immense possible effect primarily as agrochemicals, medicinal drugs, etc. D-glucosamine Derivatives, thiazole derivatives, Oxadiazolines derivatives, Quinoline derivatives, Triazol derivatives, Quinoxalines derivatives, Thiazolidinyl Derivatives, Phenoxyacetamide Derivatives, Benzimidazole derivatives, Mercapto benzimidazole derivatives, Benzoxazoles derivatives are given in this review for its reported microbial activities.Thus, the article is dedicated to the place of different thiazine ring systems in heterocycles for their nature as antimicrobial agents. The objective of this review is gather data on antimicrobial activities of thiazines derivatives. This review has clearly confirmed that substituted thiazines treated as potential antimicrobial agents. Thus, we have decided to review on different form of substituted thiazines.

2. Antimicrobial activities of various chemical derivatives

2.1. Antimicrobial activity of chitosan derivatives

Chitosan, which is derived from a deacetylation reaction of chitin, has attractive antimicrobial activity. However, chitosan applications as a biocide are only effective in acidic medium due to its low solubility in neutral and basic conditions. Also, the positive charges carried by the protonated amine groups of chitosan (in acidic conditions) that are the driving force for its solubilization are also associated with its antimicrobial activity. Therefore, chemical modifications of chitosan are required to enhance its solubility and broaden the spectrum of its applications, including as biocide. Quaternization on the nitrogen atom of chitosan is the most used route to render water-soluble chitosan-derivatives, especially at physiological pH conditions. Recent reports in the literature demonstrate that such chitosan-

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derivatives present excellent antimicrobial activity due to permanent positive charge on nitrogen atoms side-bonded to the polymer backbone. This review presents some relevant work regarding the use of quaternized chitosan-derivatives obtained by different synthetic paths in applications as antimicrobial agents[1].

2.2. D-glucosamine Derivatives

6-Sulfo-6-deoxy-D-glucosamine (GlcN6S), 6-sulfo-6-deoxy-D-glucosaminitol (ADGS) and their N-acetyl and methyl ester derivatives have been synthesized and tested as inhibitors of enzymes catalyzing reactions of the UDP-GlcNAc pathway in bacteria and yeasts. GlcN6S and ADGS at micromolar concentrations inhibited glucosamine-6-phosphate (GlcN6P) synthase of microbial origin. The former was also inhibitory towards fungal GlcN6P N-acetyl transferase, but at millimolar concentrations. Both compounds and their N-acetyl derivatives exhibited antimicrobial in vitro activity, with MICs in the 0.125-2.0 mg mL-1 range. Antibacterial but not antifungal activity of GlcN6S was potentiated by D-glucosamine and a synergistic antibacterial effect was observed for combination of ADGP and a dipeptide Nva-FMDP[2].

2.3. Thiazole derivatives

In this work, we reported the synthesis and evaluation of antibacterial and antifungal activities of three new compound series obtained from 6-(phenyl/4- chlorophenyl)imidazo[2,1-b]thiazole-3-acetic acid hydrazide: 2-{[6-(phenyl/4-chlorophenyl)imidazo[2,1-b]thiazol-3-yl]acetyl}-N-alkyl/arylhydrazinecarbothioamides (2a-d), 4-alkyl/aryl-2,4-dihydro-5-{[6-(phenyl/4-chlorophenyl)imidazo[2,1-b]thiazol-3- yl]methyl}-3H-1,2,4-triazole-3-thiones (3a-n), and 2-alkyl/arylamino-5-{[6-(phenyl/4- chlorophenyl)imidazo[2,1-b]thiazol-3-yl]methyl}-1,3,4-thiadiazoles (4a-g)[3].

The increasing clinical importance of drug-resistant fungal and bacterial pathogens has lent additional urgency to microbiological research and new antimicrobial compound development. For this purpose, new thiazole derivatives of triazoles were synthesized and evaluated for antifungal and antibacterial activity. The reaction of propionic acid hydrazides with various aryl/alkyl isothiocyanates gave thiosemicarbazides which furnished the mercaptotriazoles by alkali cyclization. The 4-phenyl/cyclohexyl-5-(1- phenoxyethyl)-3-[N-(2-thiazolyl)acetamido]thio-4H-1,2,4-triazole derivatives were synthesized by reacting the mercaptotriazoles with 2-chloro-N-(2-thiazolyl)acetamide. The chemical structures of the compounds were elucidated by IR, 1H-NMR, FAB+-MS spectral data. Their antimicrobial activities against *Candida albicans* (two strains), *Candida glabrata*, *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa* were investigated. The results showed that some of the compounds have very strong antifungal activity[4].

A new series of 2-substituted 4-(2,5-dichloro thienyl)-1,3-thiazoles are synthesized by the reaction of 2- bromo-1-(2,5-dichlorothien-3-yl) ethanone with thiourea and substituted thioamides. The newly synthesized compounds 4a-e are characterized by analytical (1)H NMR, (13)C NMR and mass spectral data. The newly synthesized compounds are screened for antifungal and antibacterial activities. Among them 4a and 4d exhibited good antifungal and antibacterial activities. The newly synthesized compounds are subjected to molecular docking studies for the inhibition of the enzyme l-glutamine: d- fructose-6-phosphate amidotransferase [GlcN-6-P] (EC 2.6.1.16) which is a new target for antifungals. Among the five molecules taken for docking studies 2-(8-quinolinyl)-4-(2,5-dichloro thienyl)-1,3-thiazole 4d shows minimum binding and docking energy and may be considered as good inhibitor of GlcN-6-P synthase[5].

Various N,N'-diaryl-1,3-thiazole-2,4-diamines (3a-w) were synthesized by a three steps process. The structures of the synthesized compounds were confirmed by spectral data and elemental analyses. All the synthesized compounds were tested against two bacterial strains and two fungal strains. Bacterial strains included Gram positive *Staphylococcus aureus* and Gram negativeve *Escherichia coli* and fungal strains included *Monascus purpurea* and *Penicillium citrinum*. Most of the compounds showed moderate to good antibacterial as well as antifungal activity[6].

A series of 4-alkyl/aryl-2,4-dihydro-5-((6-(4-bromophenyl)imidazo[2,1-b]thiazol-3- yl)methyl)-3H-1,2,4-triazole-3-thiones (3a-i) and 2-alkyl/arylamino-5-((6-(4- bromophenyl)imidazo[2,1-b]thiazol-3-yl)methyl)-1,3,4-thiadiazoles (4a-c) were synthesized starting from 6-(4-bromophenyl)imidazo[2,1-b]thiazole-3-acetic acid hydrazide. The newly synthesized compounds were characterized by IR, (1)H NMR, mass and elemental analysis. All compounds were tested for antibacterial and antifungal activities. The antimicrobial activities of the compounds were assessed by the microbroth dilution technique. The compounds were also evaluated for antituberculosis activity against Mycobacterium tuberculosis H37Rv (ATCC 27294). The preliminary results revealed that some of the compounds exhibited promising antimicrobial activities[7].

2.4. Oxadiazolines derivatives

A new series of 3-acetyl-2-aryl-2H/methyl-5-[3-(6-methylpyridinyl)]-2,3-dihydro-[1,3,4]-oxadiazole derivatives were synthesized from 6-methyl nicotinate through a multistep reaction sequence. The structures of newly synthesized

compounds were established on the basis of elemental analysis, IR, 1H NMR, 13C NMR and mass spectral data. Three dimensional structure of the compound 5f was further confirmed by single crystal X-ray analysis. All the synthesized compounds were screened for their antimicrobial activity and antioxidant activity. The final compounds were subjected to molecular docking studies for the inhibition of enzyme L-glutamine: D-fructose-6-phosphate amidotransferase [GlcN-6-P] (EC 2.6.1.16). The in silico molecular docking results are matching with the in vitro studies and they may be considered as good inhibitor of GlcN-6-P synthase.6-methylpyridine[8].

The worldwide development of antimicrobial resistance forces scientists to search for new compounds to which microbes would be sensitive. Many new structures contain the 1,3,4-oxadiazole ring, which have shown various antimicrobial activity, e.g., antibacterial, antitubercular, antifungal, antiprotozoal and antiviral. In many publications, the activity of new compounds exceeds the activity of already known antibiotics and other antimicrobial agents, so their potential as new drugs is very promising. The review of active antimicrobial 1,3,4-oxadiazole derivatives is based on the literature from 2015 to 2021[9].

2.5. Quinoline derivatives

Two new series of quinoline incorporated benzimidazole derivatives (4a-I and 8a-f) were synthesized from substituted aniline and isatin through multi-step reaction. 6-substituted-4-carboxyquinolines (3a,b and 7) were synthesized by multi component one pot reactions (via Doebner reaction and Pfitzinger reaction respectively) and the targeted benzimidazole derivatives were obtained by the reaction of 6- substituted-4-carboxyquinolines (3a,b and 7) with substituted aromatic diamines in acidic media. All the newly synthesized compounds were characterized by IR, NMR mass spectral study and also by C, H, N analyses. The final compounds were screened for their in-vitro antibacterial and antifungal activity by well plate method (zone of inhibition). The results revealed that, compounds 4c, 4d, 8c and 8d showed significant antibacterial activity. The compound 8b was found to be potent antifungal agent. 4a, 8a and 8f showed moderate to good antimicrobial activity as compared to the standard drugs against all tested microbial strains[10].

2.6. Triazol derivatives

A series of novel (E)-2-(4-(1H-1,2,4-triazol-1-yl)styryl)-4- (alkyl/arylmethyleneoxy)quinazoline derivatives (4a-4s) were synthesized in good to excellent yields, and their structures were fully characterized by [Formula: see text] NMR, [Formula: see text] NMR, HRMS and IR spectra. The structure of compound 4b was further confirmed via single-crystal X-ray diffraction analysis. The bioassay results indicated that compounds 4s, 4q and 4n inhibit phytopathogenic bacterium Xanthomonas axonopodis pv. citri (Xac) more potently than commercial bactericide bismerthiazol. However, not a single compound can effectively inhibit three pathogenic fungi tested at [11].

A total of eighteen 2-((2-(4-(1H-1,2,4-triazol-1-yl)phenyl)quinazolin-4-yl)oxy)-N- phenylacetamide derivatives were designed and synthesized, via hybrid pharmacophore approach. Among these compounds, chemical structure of compound 4a was unambiguously confirmed by means of single-crystal X-ray diffraction analysis. All the compounds were evaluated in vitro for their inhibition activity against several important phytopathogenic bacteria and fungi in agriculture. The obtained results indicated that several compounds demonstrated potent antibacterial activity against *Xanthomonas oryzae pv. oryz*ae (Xoo). For example, compounds 4c, 4g and 4q had EC50 values of 35.0, 36.5 and 32.4 μg/mL toward this bacterium, respectively, around 1.5 times more active than commercial bactericide bismerthiazol (EC50 = 89.8 μg/mL). Additionally, compounds 4j and 4p were found to display comparable antifungal activity against *Gloeosporium fructigenum* at 50 μg/mL, to commercial fungicide hymexazol. Finally, the relationships between antibacterial activities and molecular structures of this class of compounds were discussed in detail[12].

A series of structurally novel 3-thioether-1-(quinazolin-4-yl)-1H-1,2,4-triazol-5-amine derivatives (7a-7r) were designed and synthesized based on a pharmacophore hybrid approach, and screened for their antibacterial and antifungal activities in vitro. All the target compounds were fully characterized through [Formula: see text]H NMR, [Formula: see text]C NMR and HRMS spectra. Among them, the structure of compound 7b was further confirmed via single-crystal X-ray diffraction analysis. The obtained results indicated that several target compounds demonstrated notable inhibition activities against tested phytopathogenic bacteria, using a turbidimetric method. For example, compounds 7d, 7g and 7i exhibited EC[Formula: see text] (half-maximal effective concentration) values of 46.9, 47.8 and 43.2 μg/mL, respectively, against the bacterium *Xanthomonas axonopodis pv. citri* (Xac), which were more potent than commercial agrobactericide Bismerthiazol (56.9 μg/mL). Moreover, EC[Formula: see text] values of compounds 7a and 7h were found to be 81.6 and 93.1 μg/mL, respectively, against the bacterium *Ralstonia solanacearum* (Rs), being over twofold more active than commercial agrobactericide Thiodiazole-copper (189.6 μg/mL). Finally, some compounds displayed a certain degree of inhibition activity against tested phytopathogenic fungi at 50 μg/mL[13].

A series of novel quinazolin-4-one derivatives (7a-7n) bearing the 7-oxo-1,2,4- triazolo[1,5-a]pyrimidine moiety were designed, synthesized and evaluated for their inhibition activities against phytopathogenic bacteria and fungi in vitro. All of the target compounds were fully characterized through [Formula: see text] NMR, [Formula: see text] NMR, HRMS and IR spectra. Among these compounds, the structure of compound 7e was unambiguously confirmed via single-crystal X-ray diffraction analysis. The turbidimetric assays indicated that compounds 7b, 7d, 7g, 7k and 7n exhibited much more potent inhibition activities against the pathogen *Xanthomonas oryzae pv. oryzae* (Xoo), relative to control Bismerthiazol. Moreover, antibacterial activities of compounds 7j, 7k and 7n against the pathogen *Xanthomonas axonopodis pv. citri* (Xac) were comparable to that of control Bismerthiazol. As for the pathogen *Ralstonia solanacearum* (Rs), only compounds 7g and 7i demonstrated inhibition activities similar to control Thiadiazole-copper. Moreover, this class of compounds did not display inhibition activity against three fungi tested. The above findings indicated that quinazolin-4-one derivatives containing the 7-oxo-1,2,4-triazolo[1,5-a]pyrimidine moiety have a potential as promising candidates for the development of new and more efficient agricultural bactericides[14].

The title compounds were prepared by reacting [(4,5-diphenyl-1H-imidazol-2- yl)thio]acetic acid hydrazides 6 and 7 with aromatic aldehydes to give the corresponding hydrazones 6a-m and 7a-d or with isothiocyanates to afford the corresponding thiosemicarbazides 8a-c and 9. 8a-c and 9 were cyclized into triazoline-5-thiones 10a-c and 11 in the presence of sodium hydroxide or into 1,3,4-thiadiazoles 14a-c and 15 in the presence of sulfuric acid. On the other hand, 10c and 11 were also reacted with alkyl halides to obtain their thioether derivatives, 12a,b and 13. All the synthesized compounds were characterized by their elementary analysis and by using UV, IR, NMR and mass spectrometry. 6b, c, f, h-k, m, 7, 7d, 8c, 9, 10c, 11, 12a-b, 13, 14 and 15 were tested for antimicrobial activity, but no significant activity was observed[15].

The increasing clinical importance of drug-resistant bacterial pathogens has lent additional urgency to microbiological and antibacterial research. New indolic derivatives of triazoles, thiadiazoles and their respective open-chain thiosemicarbazides were evaluated for antibacterial and antifungal activity. The microorganisms used were the Gram-negative bacteria *Escherichia coli* ATCC 35218 and *Pseudomonas aeruginosa* ATCC 27853, the Gram-positive bacteria *Staphylococcus aureus* ATCC 25923 and Bacillus subtilis BBL 12084 and the yeasts Candida and Saccharomyces cerevisiae ATCC 2366. The most potent compounds were indole derivatives (12a-c) bearing 1,2,4-triazo- thien-5-yl moiety, which exhibit interesting antibacterial and antifungal activities[16].

Three novel series of benzimidazole derivatives namely 6-substituted 3-[1-(2-alkyl-1 H- benzimidazolyl)methyl]-1,2,4-triazolo[3,4-b][1,3,4] thiadiazoles 5a-h, 6-substituted 3-[1- (2-alkyl-1H-benzimidazolyl)methyl]-7H-1,2,4 -triazolo[3,4-b]-[1,3,4]thiadiazines 6a-j and 6-thioxo-3-[1-(2-alkyl-1H-benzimidazolyl)methyl]-5,6-dihydro-1,2,4 -triazolo[3,4-b][1,3,4]-thiadiazoles 7a, b have been prepared by cyclization of the key intermediate 1- [(4-amino-5-mercapto-4 H-1,2,4-triazol-3-yl)methyl]-2-alkyl-1 H-benzimidazoles 3a, b. Furthermore, 1-[(4-arylideneamino-5-mercapto- 4H-1,2,4-triazol-3-yl)-methyl]-2-alkyl- 1 H-benzimidazoles 4a-h have been prepared and some of them were cyclized to 6-substituted 3-[1-(2-alkyl-1H-benzimidazolyl)methyl]-1,2,4-triazolo [3,4- b][1,3,4]thiadiazoles 5d, h using thionyl chloride. The prepared compounds were tested for antimicrobial activity in vitro; they showed moderate activity[17].

Three novel series of benzimidazol derivatives were prepared. Namely; 2-alkyl-1-(4- substituted-4H-1,2,4-triazole-5-thion-3-yl)methylb enzimidazoles; 2-alkyl-1-(5- substituted amino-1,3,4-thiadiazol-2-yl)methylbenzimidazoles; and 2-alkyl-1-[(3,4- disubstituted thiazolin-2-ylidene)hydrazinocarbonyl] methylbenzimidazoles. The antimicrobial testing of the prepared compounds as well as of the key intermediate thiosemicarbazides was performed[18].

Two novel series of thiosemicarbazide derivatives were synthesized: 2-[4-(substituted thiocarbamoylhydrazinocarbonyl) phenoxymethyl]-1H-benzimidazoles and 1-benzyl-2- [4-(substituted thiocarbamoylhydrazinocarbonyl) phenoxymethyl]-1H-benzimidazoles, and cyclised to 2-[4-(4-substituted-4H-1,2,4-triazole-5-thion-3-yl)phenoxymethy]-1H- benzimidazoles and 1-benzyl-2-[4-(4-substituted-4H-1,2,4-triazole-5- 5-thion-3- yl)phenoxymethyl]-1H-benzimidazoles, respectively. The antimicrobial activity of the prepared compounds was tested[19].

Triazoles with different substituent groups are found to possess diverse applications in the field of medicine and industry. A series of 4-(substituted ethanoyl)amino-3- mercapto-5-(4-nitro)phenyl-1,2,4-triazoles (NU-1 to NU-15) were synthesized as novel antimicrobial agents starting from 4-nitrobenzoic acid. The chemical structures of these newly synthesized compounds were elucidated by IR, 1H NMR, 13C NMR, FAB+ -MS spectral data and elemental analysis. Their antimicrobial activities against *Staphylococcus aureus* (ATCC-25923), *Pseudomonas aeruginosa* (ATCC-27853), *Escherichia coli* (ATCC-8739), *Bacillus substilis* (ATCC-6633), *Candida albicans* (MTCC- 227), *Aspergillus niger* (MTCC-3323) and *Fusarium oxysporum* (MTCC-2087) were investigated [20].

Three novel series of benzimidazole derivatives namely 6-substituted 3-[1-(2-alkyl-1 H- benzimidazolyl)methyl]-1,2,4-triazolo[3,4-b][1,3,4] thiadiazoles 5a-h, 6-substituted 3-[1- (2-alkyl-1H-benzimidazolyl)methyl]-7H-1,2,4 -triazolo[3,4-b]-[1,3,4]thiadiazines 6a-j and 6-thioxo-3-[1-(2-alkyl-1H-benzimidazolyl)methyl]-5,6-dihydro-1,2,4 -triazolo[3,4-b][1,3,4]-thiadiazoles 7a, b have been prepared by cyclization of the key intermediate 1- [(4-amino-5-mercapto-4 H-1,2,4-triazol-3-yl)methyl]-2-alkyl-1 H-benzimidazoles 3a, b. Furthermore, 1-[(4-arylideneamino-5-mercapto- 4H-1,2,4-triazol-3-yl)-methyl]-2-alkyl- 1 H-benzimidazoles 4a-h have been prepared and some of them were cyclized to 6-substituted 3-[1-(2-alkyl-1H-benzimidazolyl)methyl]-1,2,4-triazolo [3,4- b][1,3,4]thiadiazoles 5d, h using thionyl chloride. The prepared compounds were tested for antimicrobial activity in vitro; they showed moderate activity[21].

4-Amino-2-[(5-arylamino-4,5-dihydro-1,3,4-thiadiazol-2-yl)methyl]-5-(4-methylphenyl)- 2,4-dihydro-3H-1,2,4-triazol-3-ones (3a-c) were obtained in acidic media via the formation of 2-[(4-amino-3-aryl-5-oxo-4,5-dihydro-1H-1,2,4-triazol-1-yl)acetyl]-N- arylhydrazinecarbothioamides (2a-c), and then, compound 3b was converted to methylated derivative, 4. The basic treatment of carbothioamide derivatives, 2a-c, afforded 4-amino-2-[(4-aryl-5-sulphanyl-4H-1,2,4-triazol-3-yl)methyl]-5-(4- methylphenyl)-2,4-dihydro-3H-1,2,4-triazol-3-ones (5a-c). The alkylation reactions of compounds 4H-1,2,4-triazol-3-ylmethyl-5-(4-methylphenyl)-2,4-dihydro-3H-1,2,4- triazol-3-one derivatives (5a-c) were performed by using methyl iodide or ethyl bromide in the presence of sodium ethoxide, while the treatment of the same intermediates, 5a- c, with aromatic aldehydes produced 2-{[4-(4-aryl)-5-sulphanyl-4H-1,2,4-triazol-3- yl]methyl}-4-(arylmethylene)amino-5-(4-methylphenyl)-2,4-dihydro-3H-1,2,4-triazol-3- ones (8a-d). The synthesis of 4-amino-(or arylideneamino)-5-(4-methylphenyl)-2-{[(4- methylpiperazin-1-yl or morpholin-4-ylethyl)methyl]-4-aryl-5-thioxo-4,5-dihydro-1H- 1,2,4-triazol-3-yl}methyl-2,4-dihydro-3H-1,2,4-triazol-3-ones (7a, b and 9) was performed by a one pot three-component Mannich reaction involving the corresponding compounds, 4-(substituted)amino-4H-1,2,4-triazol-3-ylmethyl-5-(4- methylphenyl)-2,4-dihydro-3H-1,2,4-triazol-3-one derivatives 5a, b and 8a, methylpiperazine or 2-(4-morpholino)ethylamine and formaldehyde. The newly synthesized compounds were well characterized by elemental analyses, IR, (1)H NMR, (13)C NMR and mass spectral studies. They were also screened for their microbial activities. The antimicrobial activity study revealed that some of which 2a, c, 3c, 5a-c, 8a- d showed good activity against a variety of microorganisms[22].

Acetic acid hydrazide containing 5-methyl-2-benzoxazolinone (4) was synthesized by the condensation of 2-(5-methyl-2-benzoxazolinone-3-yl)acetate with hydrazine hydrate. Thiosemicarbazide derivatives (5a-5d) were afforded by the reaction of corresponding compound 4 with substituted isothiocyanates. The cyclization of compounds 5a-5d in the presence of triethylamine resulted in the formation of compounds 6a-6d containing 1,2,4-triazole ring. On the other hand, the treatment of compounds 5a-5d with orthophosphoric acid caused the conversion of side chain of compounds 5a-5d into 1,3,4-thiadiazole ring: thus, compounds 7a-7c were obtained. The treatment of compound 4 with aromatic aldehydes resulted in the formation of arylidene hydrazides as cis-trans conformers (8a-8e). The structures of the compounds were elucidated by spectral and elemental analysis. While most compounds were exhibiting high activity in the analgesic-anti-inflammatory field, most of them were found to be inactive against bacteria and fungi[23].

2.7. Quinoxalines derivatives

A number of new symmetrically and asymmetrically 2,3-disubstituted quinoxalines were synthesized through functionalization of 2,3-dichloroquinoxaline (2,3-DCQ) with a variety of sulfur and/or nitrogen nucleophiles. The structures of the obtained compounds were established based on their spectral data and elemental analysis. The antimicrobial activity for the prepared compounds was investigated against four bacterial species and two fungal strains. The symmetrically disubstituted quinoxalines 2, 3, 4, and 5 displayed the most significant antibacterial activity, while compounds 6a, 6b, and the pentacyclic compound 10 showed considerable antifungal activity. Furthermore, compounds 3f, 6b showed broad antimicrobial spectrum against most of the tested strains[24].

In this study, certain 3-methyl-2-[4-(substituted amino carbonyl)anilino] quinoxalines, (2a-d) and (3a-d), were synthesized from the new key compound 2-[4- (ethoxycarbonyl)anilino]-3-methyl quinoxaline (1). In addition, a series of 2-[4-(arylidene hydrazinocarbonyl)anilino]-3-methyl quinoxalines (5a-e), as well as their cyclized oxadiazolinyl derivatives (6a-e), and a series of 2-[4-N2-acylhydrazinocarbonyl) anilino]- 3-methyl quinoxalines (7a-d), as well as their cyclized oxadiazoiyl derivatives (8a-d) were also prepared. Some of these derivatives were evaluated for antimicrobial activity in vitro. It was found that all the selected compounds exhibit antimicrobial activity and that compound 5b had a broad spectrum of activity[25].

Three novel series of quinoxaline derivatives namely 1-substituted amino-4-phenyl- 1,2,4-triazolo[4,3-a]quinoxalines 3a-c, 2-[3,4,5-trisubstituted-2,3-dihydrothiazol-2- ylidene) hydrazono]-3-phenylquinoxalines 4a-j, 5a-e, and 2-[(3-substituted-4- oxothiazolidin-2-ylidene) hydrazone]-3-phenylquinoxalines 6a-e have been synthesized by cyclization

of the key intermediates 2-substituted thiocarbamoylhydrazino-3- phenylquinoxalines 2a-e. The prepared compounds were tested in vitro for their antimicrobial activity [26].

In this study, we aimed to synthesize some new quinoxaline derivatives bearing amide moiety and to evaluate their antimicrobial activity. A set of 16 novel compounds of N- [2,3-bis(4-methoxy/methylphenyl)quinoxalin-6-yl]-substituted benzamide derivatives were synthesized by reacting 2,3-bis(4-methoxyphenyl)-6-aminoquinoxaline or 2,3-bis(4-methylphenyl)-6-aminoquinoxaline with benzoyl chloride derivatives in tetrahydrofuran and investigated for their antimicrobial activity. The structures of the obtained final compounds were confirmed by spectral data (IR, (1)H-NMR, (13)C-NMR and MS). The antimicrobial activity of the compounds were determined by using the microbroth dilution method. Antimicrobial activity results revealed that synthesized compounds exhibited remarkable activity against *Candida krusei* (ATCC 6258) and *Candida parapsilosis* (ATCC 22019)[27].

2.8. Thiazolidinyl Derivatives

A series of 7-(2-substituted phenylthiazolidinyl)-benzopyran-2-one derivatives have been synthesized by reaction of 7-amino-4-methyl-benzopyran-2-one (1) with an appropriate substituted aldehydes to obtain various Schiff bases (3a-k) which on treatment with thioglycolic acid afforded the title compounds (4a-k). Purity of the compounds has been confirmed by TLC. Structure of these compounds were established on the bases IR, 1H NMR, 13C NMR and Mass spectral data. Schiff bases and title compounds were evaluated for antibacterial and antifungal activities against various bacterial and fungal strains. The results showed that compounds 3d, 3f, 4d, 4f and 4i (100 microg/ml) exhibited good antibacterial and antifungal activity as that of standard antibiotics Ciprofloxacin and Griseofulvin[28].

2-[(2,6-Dichlorophenyl)amino]phenylacetic acid (A) on reaction with thionyl chloride gave corresponding acid chloride (B). A series of (4-oxo-thiazolidinyl) sulfonamides of quinazolin-4(3H)ones (4a-l) were prepared from Schiff bases (3a-l) of 2-[2-(2,6- dichlorophenyl)amino]phenylmethyl-3-[(4-aminophenyl)sulfonamido-1-yl]quinazolin- 4(3H)one (D) and substituted aromatic aldehyde. Newly synthesized compounds have been examined on the basis of elemental analysis, IR, 1H NMR and 13C NMR spectra. Antibacterial activity (minimum inhibitory concentration - MIC) against Gram-positive (S. aureus & S. pyogeneus) and Gram-negative (*P. aeruginosa* and *E. coli*) bacteria, as well as antifungal acivities (MIC) against C. albicans, A. niger and A. clavatus were determined by broth dilution method. Some of the compounds were endowed with a remarkable antibacterial as well as antifungal acivities[29].

Disubstituted 1,3,4-oxadaiazoles (4a-z, 4a'-f'), Mannich bases (6a-p) and S-alkylated derivatives (7a-t) have been synthesized from 2-(aryloxymethyl)benzoic acids (1a-d) through a multi-step reaction sequence. The structures of new compounds were established on the basis of their elemental analyses, IR, (1)H NMR, (13)C NMR and mass spectral data. All the synthesized compounds were screened for their in vitro antibacterial and antifungal activity and some of them exhibited good activity[30].

The long-chain alkenoic acid hydrazides (1a-d) on reaction with phenylisocyanate and phenylthiocyanate gave their corresponding semicarbazides (2a-d) and thiosemicarbazides (4a-d), which on further refluxing with POCl(3) and Ac(2)O yielded corresponding 1,3,4-oxadiazoles (3a-d) and thiadiazoles (5a-d), respectively. The structure elucidation of synthesized compounds is based on the elemental analysis and spectral data (IR, (1)H NMR, (13)C NMR and MS). The synthesized oxadiazoles and thiadiazoles have been screened for antibacterial and antifungal activities. The investigation of antimicrobial screening revealed that compounds 3c, 3d, 5c, 5d and compounds 3b, 5b, showed good antibacterial and antifungal activities, respectively[31].

Some new 3-acetyl-5-(3-chloro-1-benzo[b]thiophen-2-yl)-2-substituted phenyl-2,3- dihydro-1,3,4-oxadiazoles and 2-(3-chloro-1-benzo[b]thiophen-2-yl)-5-substituted phenyl-1,3,4-oxadiazoles have been synthesized and evaluated for antimicrobial activity. Initially, 3-chloro-1-benzo[b]thiophene-2-carbonyl chloride (1) was prepared from cinnamic acid in the presence of chlorobenzene and thionyl chloride. This compound (1) was treated with hydrazine hydrate to afford 3-chloro-1-benzo[b]thiophene-2- carbohydrazine (2) which was further reacted with various aromatic aldehydes to yield hydrazones (3a-h). Further reaction of these hydrazones (3a-h) with acetic anhydride gave 3-acetyl-5-(3-chloro-1-benzo[b]thiophen-2-yl)-2-substituted phenyl-2,3-dihydro- 1,3,4-oxadiazoles (4a-h). Reaction of the same compounds (3a-h) in the presence of chloramine-T afforded 2-(3-chloro-1-benzo[b]thiophen-2-yl)-5-substituted phenyl- 1,3,4-oxadiazoles (5a-h). The structures of newly synthesized compounds (4a-h) and (5a- h) have been confirmed by spectroscopic techniques such as IR, 1H NMR and elemental analysis. All the compounds were screened for their antibacterial activities against *Staphylococcus aureus*, *Bacillus subtilis*. *Escherichia coli* and *Pseudomonas aeruginosa* and for antifungal activity against *Candida albicans* and *Asperigillus niger*. The compounds exhibited significant antibacterial and moderate antifungal activities. Compounds 4c and 4e were found to be most potent with activities, even better than standard drug ciprofloxacin against *S. aureus* and *B. subtilis*[32].

2.9. Phenoxyacetamide Derivatives

New N-(5-methylisoxazol-3-yl)-2 or 3 or 4-(phenoxyacetamido)benzamides 6a-t were synthesized and tested for their in vitro antimicrobial activity against gram positive (*Staphylococcus aureus* ATCC 25923) and gram negative (*Escherichia coli* ATCC 25922 and *Pseudomonas aeruginosa* ATCC 27853) bacteria as well as fungi (*Candida albicans* ATCC 10231, *Candida tropicalis* ATCC 13803 and *Cryptococcus neoformans* ATCC 90112). Compounds 6 were devoid of antibacterial as well as antifungal activities at maximum tested concentrations of 50 micrograms/ml for bacteria and 100 micrograms/ml for yeast[33].

A series of novel substituted 1-(4-methoxybenzyl)-3-cyclopropyl-1H-pyrazol-5-amine benzamides 9(a-h) were synthesized to determine their antibacterial and antifungal activities as well as possible structure-activity relationships (SARs) to improve therapeutic efficacy. The pyrazol-5-amine benzamides were screened for their antibacterial activity against standard strains of Gram-positive (*Streptococcus pyogenes* NCIM 2608, *Staphylococcus aureus* ATCC 29737, *Bacillus subtilis* NCIM 2010) and Gram- negative (*Escherichia coli* ATCC 25922, *Pseudomonas aeruginosa* ATCC 20852, *Klebsiella pneumoniae* MTCC 618) bacteria by using streptomycin as positive control. They were also tested for their antifungal activities against mycotoxic strains of *Fusarium verticillioides*, *Aspergillus ochraceous*, *Aspergillus flavus, Alternaria alternata,* and *Penicillium chrysogenum* using nystatin as positive control. Among the synthesized compounds, 9d, 9g [34].

This paper describes the in vitro evaluation of antibacterial, antifungal and genotoxic activities of a series of 2,2'-dicarboxamidodiphenyldisulfides. All the studied compounds exhibited antibacterial activity against Bacillus subtilis. Most compounds were also active against *Staphylococcus aureus*. Several compounds were active against *Saccharomyces cerevisiae* and, in most cases, also against *Candida tropicalis*. No effects were observed against *Escherichia coli* or *Aspergillus niger*. Antimicrobial activity turned out to be affected by the substituent in the benzene ring and structure-activity relationships were found. The antibacterial and antifungal activities of the studied derivatives were compared with those of the corresponding 1,2-benzisothiazolin-3-ones and in some cases strong differences were observed. None of the tested compounds contained alerting groups or showed genotoxic properties[35].

The peptide LYS-[TRP(6)]-Hy-A1 (Lys-a1) is a synthetic derivative of the peptide Hy-A1, initially isolated from the frog species *Hypsiboas albopunctatus*. According to previous research, it is a molecule with broad antimicrobial activity. The objective of this study was to evaluate the antimicrobial activity of the synthetic peptide Lys-a1 (KIFGAIWPLALGALKNLIK-NH2) on the planktonic and biofilm growth of oral bacteria. The methods used to evaluate antimicrobial activity include the following: determination of the minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) in microtiter plates for growth in suspension and quantification of biomass by crystal violet staining and counting of colony forming units for biofilm growth. The microorganisms *Streptococcus oralis*, *Streptococcus sanguinis, Streptococcus parasanguinis, Streptococcus salivarius, Streptococcus mutans* and *Streptococcus sobrinus* were grown in Brain Heart Infusion broth at 37 °C under atmospheric pressure with 10% CO_2. The peptide was solubilized in 0.1% acetic acid (v/v) at various concentrations (500-1.9 μg mL(-1)). Chlorhexidine gluconate 0.12% was used as the positive control, and BHI culture medium was used as the negative control. The tested peptide demonstrated a remarkable antimicrobial effect, inhibiting the planktonic and biofilm growth of all strains tested, even at low concentrations. Thus, the peptide Lys-a1 is an important source for potential antimicrobial agents, especially for the control and prevention of microbial biofilms, which is one of the most important factors in cariogenic processes[36].

Although chlorhexidine is one of the most efficacious antimicrobial agents used for the prevention of dental caries, side effects limit its application. The effects of gaegurin 6 (GGN6), an animal-derived cationic peptide, and its derivatives PTP6 and PTP12 on the growth of oral streptococci were investigated to assess the potential of these agents for use in the prevention of dental caries. The minimal inhibitory concentrations of the peptides for inhibition of the growth of oral streptococci (*Streptococcus mutans* , *S. sobrinus*, *S. sanguis* and *S. gordonii*) ranged from 1.2 to 8.2 muM. The peptides also exhibited marked synergistic antibacterial effects with chlorhexidine or xylitol. The most effective combinations (fractional inhibitory concentration index of 0.5) were xylitol with GGN6 against *S. gordonii* 10558 and chlorhexidine with either GGN6 or PTP6 against *S. sobrinus* OMZ-175. These results indicate that cationic peptides alone or in combination with chlorhexidine or xylitol might prove effective for the inhibition of the growth of cariogenic oral streptococci in situ[37].

The aim of this study was to investigate the antimicrobial activity of vanadium chloroperoxidase (VCPO) reaction products on planktonic and biofilm cells of *Streptococcus mutans* C180-2. Planktonic and biofilm cells were incubated

in a buffered reaction mixture containing VCPO, halide (either chloride or bromide) and hydrogen peroxide, and the killing efficacy was assessed by CFU counts. The enzymatic products formed by VCPO significantly reduced the viability of planktonic and biofilm cells compared to their negative controls and the effect on the biofilm cells was more effective than a 0.2% chlorhexidine digluconate treatment. We conclude that VCPO and its reaction products form a potent antimicrobial system against *S. mutans*[38].

To determine the minimal inhibitory concentrations (MICs) of bacteriocin PsVP-10, chlorhexidine and triclosan on *S. mutans* and *S. sobrinus* and to study the potential synergistic combination between these antimicrobial and the bacteriocin PsVP-10. Were determined MICs of bacteriocin PsVP-10, triclosan and chlorhexidine on strains of *S. mutans* and *S. sobrinus*, which formed a biofilm or did not form a biofilm. In addition, the synergistic effect was analysed by the determination of respective fractionary inhibitory concentrations (FICs) between bacteriocin PsVP-10 plus chlorhexidine and bacteriocin PsVP-10 plus triclosan. MICs of three antimicrobials used were higher in those bacterial strains, which formed a biofilm. An interesting synergistic effect on both studied species was observed when bacteriocin and chlorhexidine were combined. A slighter synergy was determined for the combination bacteriocin PsVP-10 and triclosan. The results showed that the combination of chlorhexidine bacteriocin PsVP-10 could reduce the number of cariogenic bacteria for in vitro studies. In the future this synergistic combination could be an alternative to antimicrobial therapy against S. mutans or *S. sobrinus*[39].

In diagnostic microbiology, culture media are widely used for detection of pathogenic bacteria. Such media employ various ingredients to optimize detection of specific pathogens such as chromogenic enzyme substrates and selective inhibitors to reduce the presence of commensal bacteria. Despite this, it is rarely possible to inhibit the growth of all commensal bacteria, and thus pathogens can be overgrown and remain undetected. One approach to attempt to remedy this is the use of "suicide substrates" that can target specific bacterial enzymes and selectively inhibit unwanted bacterial species. With the purpose of identifying novel selective inhibitors, six novel phosphonopeptide derivatives based on d/l-fosfalin and β-chloro-l-alanine were synthesized and tested on 19 different strains of clinically relevant bacteria. Several compounds show potential as useful selective agents that could be exploited in the recovery of several bacterial pathogens including Salmonella, *Pseudomonas aeruginosa*, and Listeria[40].

2.10. Antimicrobial activity of the indolicidin

Natural peptides with antimicrobial activity are extremely diverse, and peptide synthesis technologies make it possible to significantly improve their properties for specific tasks. Here, we investigate the biological properties of the natural peptide indolicidin and the indolicidin-derived novel synthetic peptide In-58. In-58 was generated by replacing all tryptophan residues on phenylalanine in D-configuration; the α-amino group in the main chain also was modified by unsaturated fatty acid. Compared with indolicidin, In- 58 is more bactericidal, more resistant to proteinase K, and less toxic to mammalian cells. Using molecular physics approaches, we characterized the action of In-58 on bacterial cells at the cellular level. Also, we have found that studied peptides damage bacterial membranes. Using the *Escherichia coli* luminescent biosensor strain MG1655 (pcolD'::lux), we investigated the action of indolicidin and In-58 at the subcellular level. At subinhibitory concentrations, indolicidin and In-58 induced an SOS response. Our data suggest that indolicidin damages the DNA, but bacterial membrane perturbation is its principal mode of action[41].

2.11. Benzimidazole derivatives

In this study 12 novel benzimidazole compounds bearing hydrazone moiety were synthesized in order to investigate their possible antibacterial and antifungal activity. Structures of the synthesized compounds were elucidated by spectral data. Six different gram-negative and four different gram-positive bacterial strains were used in antibacterial activity tests. Antifungal activity tests were also performed against three different fungal strains. Most of the test compounds found to be significantly effective against *Proteus vulgaris*, *Staphylococcus typhimurium*, *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* gram-negative bacterial strains. A structure-activity relationship (SAR) study including some electronic parameters was carried out and a connection between antibacterial activity and electronic properties of the target compounds was determined. Toxicity of the most effective compounds was established by performing Brine-Shrimp lethality assay. (NCTC 5310) as yeast like fungi. The most potent compound was the pyrazolone 6a which exhibits interesting antibacterial activity against the gram-negative bacteria *E. coli*[42].

Four novel series of pyrazolylbenzimidazole derivatives have been prepared, namely 2- [(1-substituted phenyl-3,5-dimethyl-4-pyrazolyl)methyl]benzimidazole 5a-d 2-[(1- substituted phenyl-3-methyl-5-oxo-4,5-dihydro-4-pyrazolyl-4-yl)methyl]benzimidazoles 6a-d; 2-[(1-substituted phenyl-3,5-dioxopyrazolidin-4-yl)methyl]benzimidazoles 7a-d and 2-[(4-(1-phenyl-5-aryl-4,5-dihydro-3-pyrazolyl)phenylaminoacetyl]thio- methyl)- benzimidazoles 12a-e. The antimicrobial testing of the prepared compounds was performed using *Escherichia coli* (NCTC 5933) as Gram-negative bacteria, *Staphylococcus aureus* (NCTC 4163) as gram-positive bacteria and *Candida albicans*[43].

In the present study a new series of benzimidazole derivatives bearing various (benz)azolylthio moieties were synthesized so as to investigate their antimicrobial activity. Structures of the target compounds (5a-5i) were confirmed by their IR, (1) H- NMR, ES-MS spectral data, and elemental analyses. The synthesized compounds (5a-5i) exhibited poor activity against bacterial strains. On the other hand, antifungal activity of the compounds against Candida species was very significant. Brine-Shrimp lethality assay was performed for determination of toxicity of the compounds. Compounds 5a, 5c, and 5d were evaluated as non-toxic in addition to their attractive antifungal activity. However, the other compounds (5b, e-i) in the series showed toxicity to different extents[44].

Some derivatives of benzimidazole were synthesized by nucleophilic substitution of 2- substituted-1H-benzimidazole. The resulting ethyl (2-substituted-1H-benzimidazol-1-yl) acetate on treatment with hydrazine hydrate yielded 2-(2-substituted-1H-benzimidazol- 1-yl) acetohydrazide, which on further reaction with one equivalent of different aliphatic or aromatic carboxylic acids in the presence of phosphoryl chloride afforded the corresponding target compounds, 2-substituted-1-[{(5-substituted alkyl/aryl)-1,3,4- oxadiazol-2-yl} methyl]-1H-benzimidazole. The structures of the synthesized compounds were evaluated by spectral and elemental methods of analyses. All the synthesized compounds were screened for their antimicrobial activities. All of the derivatives showed good activity towards Gram-positive bacteria and negligible activity towards Gram-negative bacteria. Some of the synthesized compounds showed moderate activity against tested fungi[45].

A series of novel 2-(1H-benzimidazol-2-ylsulfanyl)-N-(4-oxo-2-phenyl-thiazolidin-3yl)- acetamide 5a-j have been synthesized from various aldehydes and 2-(5-phenyl-[1,3,4]- oxadiazol-2-ylmethylsulfanyl)-1H-benzimidazole 6a-j from various benzoic acids. These compounds were screened for their in-vitro anti-bacterial activity against *Staphylococcus aureus* and *Enterococcus faecalis* as Gram positive, *Klebsiella pneumoniae* and *Escherichia coli* as Gram negative bacterial strains and for in-vitro anti- fungal activity against *Asperigillus fumigatus* and *Candida albicans*. The in vitro cytotoxic properties were studied using brine shrimp bioassay. Results revealed that, compounds 5b, 5d, 5g, 5i, 6b, 6e, 6f, and 6i showed excellent activity against a panel of microorganisms. The cytotoxic activities of 5b, 5g, 5i, 6b, 6f, 6h, and 6i were found to be good. All the newly synthesized compounds were characterized by elemental analysis, IR, (1)H-NMR, (13)C-NMR and MS[46].

2.12. Mercapto benzimidazole derivatives

A series of novel 2-(1H-benzimidazol-2-ylsulfanyl)-N-(4-oxo-2-phenyl-thiazolidin-3yl)- acetamide 5a-j have been synthesized from various aldehydes and 2-(5-phenyl-[1,3,4]- oxadiazol-2-ylmethylsulfanyl)-1H-benzimidazole 6a-j from various benzoic acids. These compounds were screened for their in-vitro anti-bacterial activity against *Staphylococcus aureus* and *Enterococcus faecalis* as Gram positive, *Klebsiella pneumoniae* and *Escherichia coli* as Gram negative bacterial strains and for in-vitro anti- fungal activity against *Asperigillus fumigatus* and *Candida albicans*. The in vitro cytotoxic properties were studied using brine shrimp bioassay. Results revealed that, compounds 5b, 5d, 5g, 5i, 6b, 6e, 6f, and 6i showed excellent activity against a panel of microorganisms. The cytotoxic activities of 5b, 5g, 5i, 6b, 6f, 6h, and 6i were found to be good. All the newly synthesized compounds were characterized by elemental analysis, IR, (1)H-NMR, (13)C-NMR and MS[47].

A new series of novel 5-(nitro/bromo)-styryl-2-benzimidazoles (1-12) has been synthesized by simple, mild and efficient synthetic protocol by attempted condensation of 5-(nitro/bromo)-o-phenylenediamine with trans-cinnamic acids in ethylene glycol. Screening for in vitro anti-tubercular activity against Mycobacterium tuberculosis H(37) Rv, anti-bacterial activity against *Staphylococcus aureus*, *Escherichia coli*, *Enterococcus faecalis*, *Klebsiella pneumoniae* bacterial strains and anti-fungal activity against *Candida albicans* and *Asperigillus fumigatus* fungal strains were carried out. Compounds 5, 7, 8, 9, 11 showed higher anti-tubercular activity and compounds 7, 8, 10, 11, 12 have proved to be effective with MIC (microg/ml) and emerged as lead molecules showing excellent activities against a panel of microorganisms. All synthesized compounds were characterized using IR, (1)H, (13)C NMR, GC-MS and elemental analysis[48].

2.13. Benzoxazoles derivatives

Some new 2-(benzyl/p-chlorobenzyl)-5-[(substituted-thienyl /phenyl/ phenylthiomethyl /benzyl)carbonylamino] benzoxazole derivatives have been synthesized by reacting 5-amino-2-(benzyl/p-chlorobenzyl) benzoxazoles with appropriate carboxylic acid chlorides.

The structures of the synthesized compounds were confirmed by IR, (1)H NMR and MASS spectral data. In vitro antimicrobial activities of the compounds were investigated using twofold serial dilution technique against different two Gram-positive, two Gram-negative bacteria and three Candida spp. in comparison with standard drugs. Microbiological results indicated that the newly synthesized 2-(benzyl/p-chlorobenzyl)-5-[(substituted-

thienyl/phenyl/phenylthiomethyl/benzyl)carbonylamino]benzoxazole derivatives (3-12) possessed a broad spectrum of activity having MIC values of 6.25-100 microg/ml against the tested microorganisms. Especially, with an MIC value of 6.25 microg/ml, 2- (p-chlorophenyl)-5-[(2,5-dimethylphenyl)carbonylamino]benzoxazole 4 displayed the same activity against *Candida albicans* as the standard drug clotrimazole[49].

In this study, a series of twelve novel 5-[2-(morpholin-4-yl)acetamido] and/or 5-[2-(4- substituted pip-erazine-1-yl)acetamido]-2-(p-substituted phenyl]benzoxazole derivatives have been synthesized and their structures were confirmed by IR, (1)H NMR, and mass spectral data. These compounds were prepared by reacting 5-(2-chloroacetamido)-2-(4-p-substituted-phenyl)benzoxazoles, which were obtained by using 5-amino-2-[p-substituted-phenyl]benzoxazoles with chloroacetyl chloride, in the presence of morpholine or 1-substituted piperazines. All synthesized compounds 3-14 were tested by using the method of twofold serial dilution technique for in vitro activities against certain strains of Gram-positive, Gram-negative bacteria as well as the yeasts *Candida albicans*, Candida krusei, and *Candida glabrata* in comparison with standard drugs. Microbiological results showed that the newly synthesized compounds possessed a broad spectrum of activity, showing MIC values of 3.12-50 mug/mL against the Candida species[50].

The synthesis and antimicrobial activity of a new series of 2-(substitutedphenyl/benzyl)- 5-[(2-benzofuryl)carboxamido]benzoxazole derivatives 3-12 were described. The in vitro antimicrobial activity of the compounds was determined against some Gram-positive, Gram-negative bacteria and fungi and their drug-resistant isolates in comparison with standard drugs. Antimicrobial results indicated that the synthesized compounds possessed a broad spectrum of activity with MIC values 500-15.625 microg/ml. In the series, the most active compound against Candida krusei and *Candida albicans* isolate is 8 with MIC value 31.25 microg/ml. However, it is one dilution less potent than the compared fluconazole. Some of the screened compounds exhibit significant activity, having MIC value as 31.25 microg/ml in *Pseudomonas aeruginosa* having same activity as Rifampicin. Furthermore, considering the worth of developing new antibacterial agents against drug-resistant *P. aeruginosa* the present study explores the structure-activity relationship analysis of 2-(substitutedphenyl/benzyl)-5-[(2- benzofuryl)carboxamido]benzoxazoles using 3D-common features pharmacophore hypotheses approach[51].

In this study, a new series of 2,5-disubstituted benzoxazoles was synthesized and their structures were elucidated by elemental analysis, MASS, (1)H-NMR, (13)C-NMR and IR spectral data. Newly and previously synthesized 2,5-disubstituted benzoxazole derivatives were evaluated for antibacterial and antifungal activity against standard strains and their drug-resistant isolates. Microbiological results showed that the compounds presented a large spectrum of activity having MIC values of 250-7.8 microg mL(-1) against the tested microorganisms. Among the newly synthesized derivatives 3- 22, compound 11 was the most active against Candida krusei out of all; however, it was one dilution less potent than standard drug fluconazole. In addition, all the new and previous compounds were more active than standard drugs ampicillin trihydrate and rifampicin against *Pseudomonas aeruginosa* and its gentamicin-resistant isolate. The 2D-QSAR (Quantitative Structure-Activity Relationship) analysis of a set of newly and previously synthesized benzoxazoles tested for growth inhibitory activity against methicillin-resistant *Staphylococcus aureus* (MRSA) was also performed by using multivariable regression analysis. The activity contributions for substituent effects of these compounds were determined from the correlation equation for predictions of the lead optimization[52].

New ethyl 3,4-dihydro-3-oxo-4,6,7-trisubstituted-2H-1,4-benzoxazine-2-acetate derivatives were synthesized and their structures were elucidated by IR, (1)H NMR and mass spectral data. Antimicrobial activity of the compounds was investigated by using the method of twofold serial dilution technique against different Gram-positive, Gram- negative bacteria and some Candida species in comparison to standard drugs. Microbiological results indicated that the synthesized compounds possessed a broad spectrum of activity having MIC values of 6.25-100 micro g/ml against the tested microorganisms. The QSAR analysis of a set of these compounds tested for growth inhibitory activity against Candida krusei was performed by using the computer-assisted multiple regression procedure. The activity contributions for substituent effects of these compounds were determined from the correlation equation for predictions of the lead optimization[53].

3. Conclusion

In this review, the antibacterial activities of various novel chemical derivatives such as naphthoquinones, benzoquinones, anthraquinones are designated. The antibacterial activity of D-glucosamine Derivatives, thiazole derivatives, Oxadiazolines derivatives, Quinoline derivatives, Triazol derivatives, Quinoxalines derivatives, Thiazolidinyl Derivatives, Phenoxyacetamide Derivatives, Benzimidazole derivatives, Mercapto benzimidazole derivatives, Benzoxazoles derivatives were enhanced due to the polarity of the substituents: the stronger polarity, the excellent antibacterial activity against various gram-positive and negative bacteria and pathogens. This summary and

review of antibacterial activities of various chemical derivatives deliver notable supervision for additional design and synthesis of chemical derivatives and their related drugs.

Compliance with ethical standards

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Disclosure of conflict of interest

No any conflict of interest.

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