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Antimicrobial potential of hydrazone scaffold

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Abstract
Discovery of new chemical entities as efficient and non-toxic chemotherapeutic agents is the only way to overcome the challenging problems of infectious microbial diseases which exist due to emergence of multi-resistant microbial pathogens. Synthetic flexibilities and the chemotherapeutic value associated with hydrazones make itself a privileged pharmacophore in the field of medicine. In order to pave the way for future advanced research, there is a urgent need to collect and analyze the most recent information existing so far in this promising area. This review collected the recent literature reports specifically on antimicrobial potential of hydrazone derivatives which may helpful for the researcher in the field of new drug discovery and development.

Keywords: hydrazone, antimicrobial activity, antibacterial activity, antifungal activity

Introduction
Infectious microbial diseases still remain important and challenging problems [1-4] at the global level, because of emergence of an increased number of multi-drug (β-lactam antibiotics, macrolides, quinolones and vancomycin) resistant [5-7] microbial pathogen among variety of clinically significant species of microorganisms. One way to get rid of this problem is the conscious usage of the currently available antibiotics, the other way is the development of novel compounds particularly more potent anti-microbial activities. Hence, in the present drug research area, there will always be a vital need to discover new chemotherapeutic agents endowed with more potent antimicrobial activities, which must be different from already well-known existing class of antimicrobial agents to which many relevant pathogens are well resistant.

Hydrazones constitute a significant class of organic compounds. Hydrazone comprises azomethine group (-NH-N=CH-) which is responsible for its chemotherapeutic value [8-10] and synthetic potential in present drug research area [11-15]. They also make complexes with metal which have potential applications as catalysts, molecular sensors and luminescent probes [16-18]. Besides possessing diverse biological applications such as anticonvulsant, anticancer, antidepressant, analgesic, antiinflammatory, antiplatelet, antimalarial, antimicrobial, antimycobacterial, antitumoral, vasodilator, antiviral and antischistosomiasis etc. hydrazone and its derivative also make core structure of number of well-established marketed antibacterial drugs such as furazolidone **1**, furacilin **2** etc. In recent time, the antimicrobial activity is the most frequently encountered potential of the hydrazones and its derivatives by medicinal chemists in scientific literature.

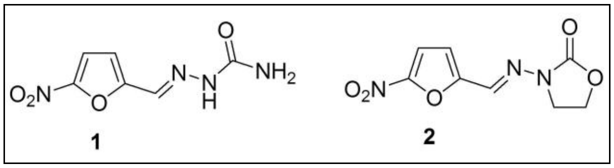

Fig 1

In view of the above observations and as combination, this present review is an attempt to collect hydrazones with antimicrobial potential

Antibacterial Activity
Özkay *et al*. [19] investigated *in vitro* evaluation of some novel benzimidazole derivatives bearing hydrazone moiety for their antimicrobial activity against Gram negative bacterial strains like *Salmonella typhimurium, Escherichia coli, Proteus vulgaris, Klebsiella pneumoniae, or Pseudomonas aeruginosa and* Gram-positive bacteriail strains like *Listeria monocytogenes, Staphylococcus aureus, Enterococcus faecalis*, *Bacillus subtilis* and reported them with significant antimicrobial activity. Among them Compound **3a-b** found to be more potent against *S. typhimurium* than the reference drug.

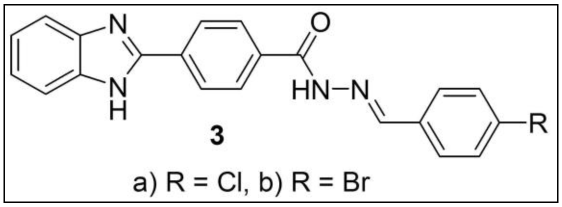

Fig 2

Noshiranzadeh *et al.* [20] synthesized and screened a series of chiral lactic-hydrazones for their antibacterial activity against *Staphylococcus aureus*, *Streptococcus pneumonia*, *Escherichia coli* and *Pseudomonas aeruginosa*. All Synthesized derivatives showed good antibacterial activity. Among synthesized compounds, (S,E)-2-hydroxy-N-(2-hydroxy-5-nitrobenzylidene) propanehydrazide **4** and (S,E)-2-hydroxy-N-((3-hydroxy-5-(hydroxymethyl)-2-methylpyridin-4-yl)propanehydrazide **5** were reported as the most potent against *S. aureus* and *E. coli*.

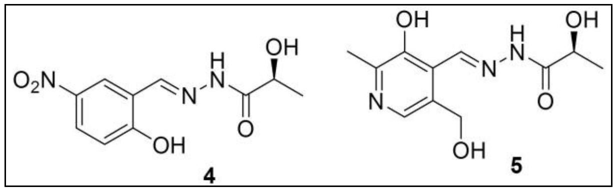

Fig 3

Zha *et al.* [21] have reported the synthesis and *in vitro* screening of some benzo[d]thiazole-hydrazones for their antibacterial potential against two *S. aureus*, *Bacillus subtilis* and *E. coli* and *K. pneumonia*. Analogues bearing electron donating groups presented showed increased antibacterial activity. Reported results also revealed that compounds **6a-e**, **7** and **8** exhibited superior antibacterial potency compared to the reference drugs chloramphenicol and rifampicin

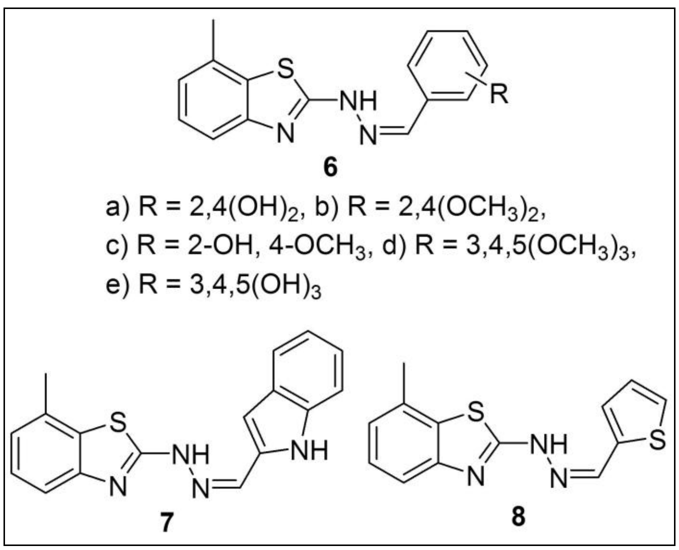

Fig 4

Xu *et al.* [22] synthesized and screened a series of novel 8-OMe-Ciprofloxacin (CPFX)-Hydrozone/Azole Hybrids for their in vitro antibacterial activity against *Staphylococcus epidermidis*, *Enterococcus faecalis* (two strains), *Stenotrophomonas maltophilia and S. aureus*,. The results show that all of the 8-OMe CPFX-hydrozone hybrids have potent activity. Compound **9** showed remarkable activity against CPFX-resistant *S. maltophilia*.

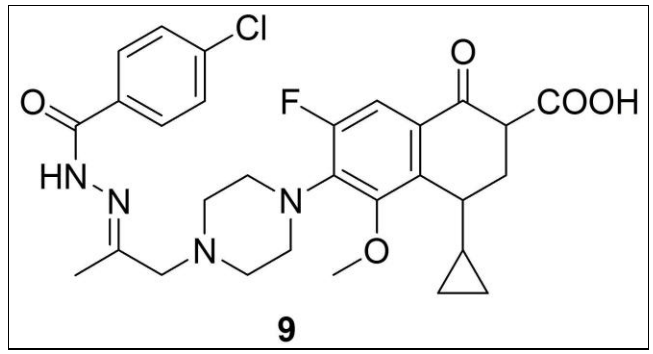

Fig 5

In another study, Asati *et al.* [23] reported the synthesis of some 1, 3-benzothiazole-2-yl-hydrazones and evaluated them for antibacterial activity against four different bacterialstrains i.e. *B. subtilis*, *E. coli*, *K. pneumoniae* and *Pseudomonas alkaligenes*. Among Compound **10a-b** found most potent derivative.

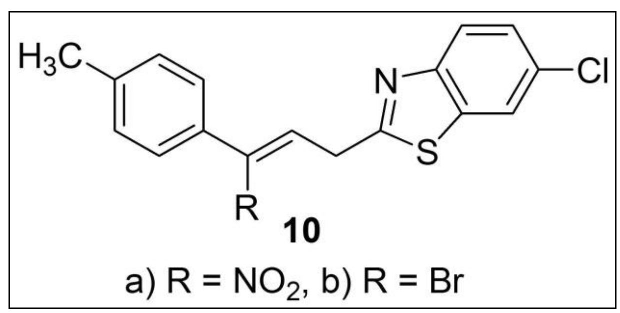

Fig 6

Osorio *et al.* [24] evaluate some newly synthesized hydrazones against methicillin-resistant *S. aureus* and reported Compounds **11** &**12** possess significant potential to inhibit the growth of *S. aureus.*

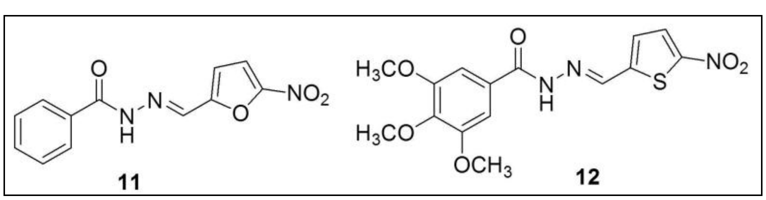

Fig 7

Ajani *et al.* [25] have reported synthesis of various 2-quinoxalinone-3-hydrazone derivativesand their biological screening against Bacillus anthracis, B. stearothermophilus (NCIB 8222), B. subtilis, Bacillus cereus, S. aureus, E. coli, P. fluorescence, K. pneumonia, Shigella dysenteriae, P. aeruginosa and compound **13** found to be most active among all synthesized derivatives.

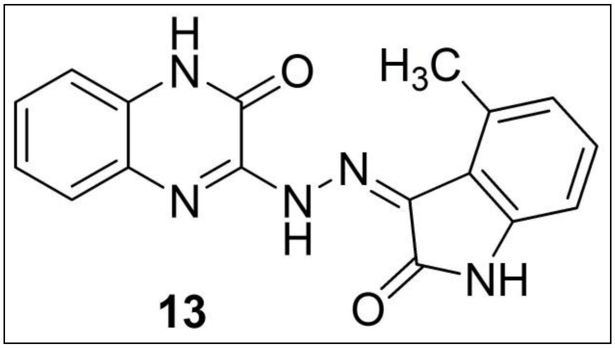

Fig 8

Eswaran *et al*. reported [26] the synthesis of a series of quinoline hydrazones **14** possessing antibacterial potency against *E. coli, S. aureus, P. aeruginosa* and *K. Pneumonia.*

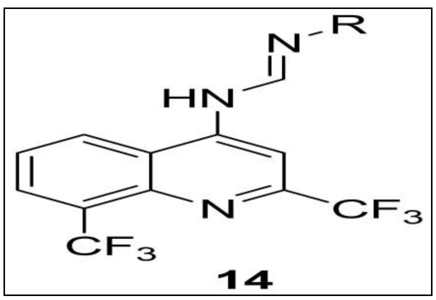

Fig 9

Antifungal Activity

Neuman *et al.* [27] reported synthetic preparations of a library of 2,4,6-pyrimidinetrione carbaldehyde hydrazones including PhenylHydrazones **15**, Acylhydrazones **16**, Benzenesulfonohydrazones **17** and their potential for inhibition of fungal growth against g *Candida albicans* and *Candida glabrata*. Mostly derivatives have shown significant potential inhibit growth of *C. albicans* and *C. glabrata*

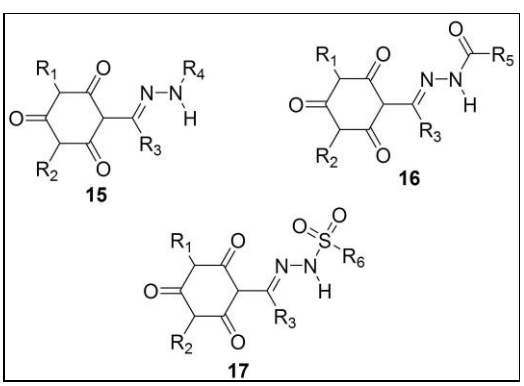

Fig 10

The antifungal activity of the salicylaldehyde hydrazones were also investigated by Backes *et al.* [28] using *C. albicans* and *C. Glabrata.* All screened salicylaldehyde hydrazone and hydrazide showed good antifungal activity through fungal growth inhibition but nitrobenzohydrazides compounds **18a-b** and halogenated benzohydrazide **19** were found most potent inhibitors of fungal growth.

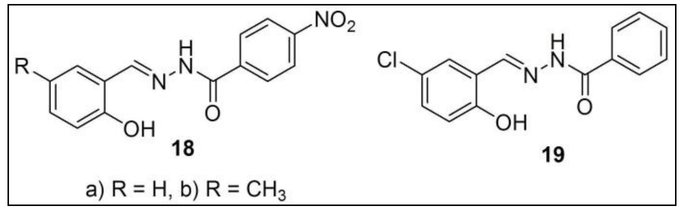

Fig 11

Zha *et al.* [21] have also reported *in vitro* screening of some newly synthesizes benzo[*d*]thiazole-hydrazones for their antifungal activity against three fungal strains such as *Aspergillus niger*, *Fusarium moniliforme* and *Fusarium oxysporum*. Compounds **20**, **7** and **8** were found to be good antifungal activity compared to the standard drug ketoconazole.

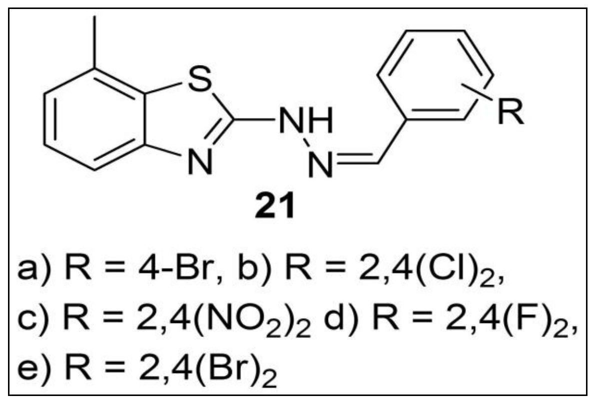

Fig 12

Kamal *et al.* [29] reported the synthesis and antifungal activities of ten novel pyrimidinyl hydrazones **22a-j**. The results revealed that all synthesized compounds were found to be more potent then reference drug to inhibit the growth of *C. albicans*.

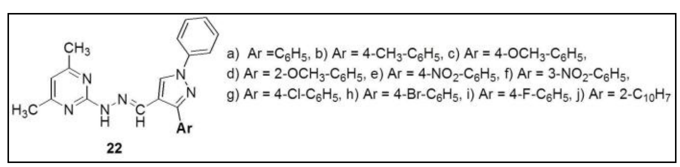

Fig 13

Casanova *et al.* have evaluated fourteen new hydrazones for their growth inhibition potential against *Candida* species (*C. parapsilosis, C. tropicalis, C. krusei, C. albicans, C. glabrata* and *C. lusitaneae*) and *Trichosporon asahii* and found that compound **23** possess most promising activity among all synthesised analogues.

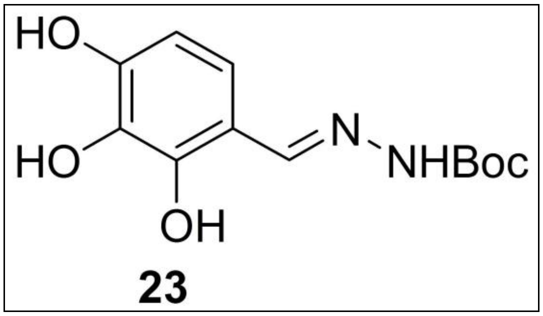

Fig 14

Shirinzadeh *et al*. synthesized and screened some indole-containing hydrazone derivatives against *C. albicans* and reported that compounds **24** and **25** possess strong inhibition potential against *C. albicans*.

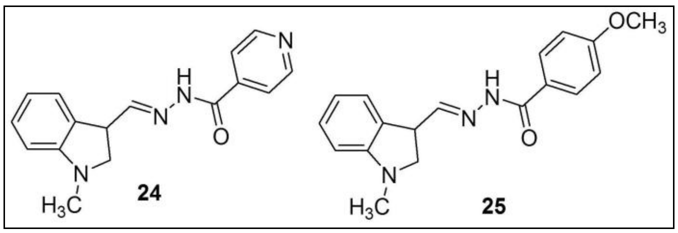

Fig 15

Conclusion

This present review is an attempt to make overview regarding the potential of the hydrazone moiety in bioactive molecules as antimicrobial agent in the field of novel drug discovery and development.

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Conflict of Interest

Authors has declared no conflict of interest.

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