PIPERAZINE: THE MOLECULE OF DIVERSE PHARMACOLOGICAL IMPORTANCE
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ABSTRACT
Piperazine nucleus is one of the most important heterocyclic exhibiting remarkable pharmacological activities. The present review provides a broad view of the pharmacological activities, antipsychotic, anticonvulsants, antiarrhythmic, antimicrobial, antioxidant, antimalarial, and cytotoxic activities possessed by compounds having piperazine nucleus.

Keywords: Piperazine, Heterocyclic, Antipsychotic, Antimicrobial and Cytotoxic.

INTRODUCTION
The practice of medicinal chemistry is devoted to the discovery and development of new agents for treating disease. An important aspect of medicinal chemistry has been to establish a relationship between chemical structure and pharmacological activity. Piperazine is consisting of a six membered ring containing two opposing nitrogen atoms. Slight change in substitution pattern in piperazine nucleus causes distinguishable difference in their pharmacological activities.

Pharmacological Activities
Antipsychotic activity
Alka Bali et al., synthesized a series of acetophenone based 1-(Aryloxypropyl)-4-(chloroaryl) piperazines. All the synthesized compounds were evaluated for atypical antipsychotic activity. All the target compounds were subjected to preliminary pharmacological evaluation to determine their ability to antagonize Apomorphine induced mesh climbing behavior and Apomorphine induced stereotype in mice. Compounds a1, a2, a3, a4, & b1, b2 shows the positive result for reversal of Apomorphine induced mesh climbing and a5, a6, a7, a8 shows negative response. Compounds a1, a2, a5, a6, a7, a8, and b1, b2 shows positive response for reversal of Apomorphine induced stereotype and a3 &a4 shows negative response. Apomorphine used as standard drug.

Sushil Kumar et al., reported the synthesis and preliminary pharmacological evaluation of 2-[4-(aryl substituted) piperazin-1-yl]-N-phenylacetamides: Potential antipsychotics. All the synthesized compounds were tested for antipsychotic activity by using models Apomorphine induced mesh climbing assay, Antagonism of 5-hydroxytryptophan induced head twitches and catalepsy.

The compounds possessing Chloro group at ortho and meta positions of aryl moiety of piperazine produced a significant greater reversal of Apomorphine induced climbing behavior than their methoxy analogs. A significant reduction in activity was observed when nitro group was present at para position of aryl moiety. Other compounds showed lower efficacy at D2 receptor.

The inhibition of 5-HTP induced head twitches study showed that methoxy analogs produced significant higher activity than chloro analogs. The other compounds showed lower antagonism of 5-HTP induced head twitches behavior.

The catalepsy results showed all the compounds were less cataleptogenic than haloperidol. Among them, Chloro analogs exhibited the lowest propensity to produce catalepsy.

R = H, 3-CH3, 4-CH3, 2-OCH3, 3-OCH3, 2-Cl, 3-Cl, 4-F, 4-NO2

Anticonvulsant activity
Mutlu Dilisz Aytemir et al., reported the synthesis and evaluation of anticonvulsant activity of 3-hydroxy-6-methyl-2-substituted 4H-pyran -4-one derivatives. Among the compounds 4-(3-trifluoromethylphenyl) piperazin-1-yl methyl group at position 2 on the pyranone ring.

Mutlu Dilisz Aytemir et al., also reported the synthesis and anticonvulsant activity of new kojic acid derivatives. Among the compounds 3-hydroxy-6hydroxyethyl-2-[4-(2-methyl phenyl) piperazin-1-yl methyl]-4-pyran-4-one was found to be highly selective and most active.

Antiarrhythmic activity
Jacek Sapa et al., reported the Antiarrhythmic activity of 1-[2-hydroxy-3-(4-phenyl-1-piperazinyl) propyl]-pyrrolidin-2-one [MG-1(R, S)] and its enantiomers. The arrhythmia was evoked in rats anesthetized with thiopental (60 mg/kg, i.p.) by intravenously injection of adrenaline in to the caudal vein (20 µg/kg in a volume of 1ml/kg) or by intravenously injection of barium chloride solution was injected into caudal vein of rats (32mg/kg in a volume of 1 ml/kg) The most active compound after oral administration was the S enantiomers.
Antimicrobial activity
Ishwar J. Patil et al., has synthesized a novel series of substituted phenylacetamide by condensing 1-(4-amino phenyl)-2-(4R,4S)-(4-chlorophenyl) (phenyl) methyl -1- piperazinyl| ethanone in presence of acid catalyst under reflux conditions. All the synthesized compounds were characterized by elemental and spectral analysis. The newly synthesized compounds were evaluated for antibacterial and antifungal activity.

Antibacterial activity: All the synthesized compounds were evaluated against gram positive bacteria (Staphylococcus aureus, Streptococcus pyogenes) and gram negative bacteria (Escherichia coli, Pseudomonas aeruginosa). The compounds containing methyl and methoxy group at position  high active against all four organism employed. All compounds except chloro and nitro containing analogs at position 2 were highly active against Escherichia coli, & Staphylococcus aureus. Ciprofloxacin, Norfloxacin, Gentamycin were used as standard drug in evaluation of antibacterial activity.

Antifungal activity: The synthesized compounds were studied against Candida albicans, Aspergillus niger. The compound shows good activity against Aspergillus niger. Greseofulvin, nystatin were used as standard drugs.

Antioxidant activity
Agata Pietrzycka et al., reported preliminary evaluation of antioxidant activity of some 1-(phenoxyethyl)-piperazine derivatives. The antioxidant profile of 1-(phenoxyethyl)-piperazine derivatives were compared to Trolox and Resveratrol. The piperazine derivatives possessing 4-(methyl) or 1-[2,6-(dimethyl)phenoxyethyl] moiety were shows significant activity.

Antimalarial activity
Wilson Cunico et al., reported (2R, 3S)-4-(aryl methyl)-1-(4-phenyl-3-amino-2-hydroxy butyl)piperazine derivatives as potential antimalarial agents.

Cytotoxic activity
Saeed Rajabalian et al., reported N-(2-oxyliminoethyl) piperazinyl quinolones as new cytotoxic agents. Cytotoxic activity of the test compounds was investigated in comparison with etopside. The compounds (a-d) indicate poor activity and compounds (e-i) showed significant activity.

Apart from these activities piperazine also possess anti-inflammatory, hypotensive etc. and also used as antiscale and corrosion additives for water treatment.

CONCLUSION
Piperazines occupy a unique place in pharmaceutical field. This heterocyclic moiety shows great pharmacological significance. The pharmacological activities of this new generation of piperazine represent much progress with regard to older compounds.

REFERENCES