

REVIEW OF LITERATURE OF INDOLE DERIVATIVES AGENTS

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ABSTRACT

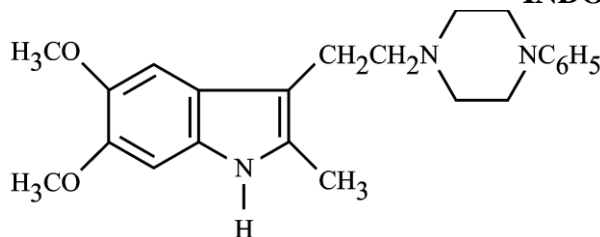
Psychotropic agents can be placed into 4 major categories. Antianxiety-sedative agents particularly benzodiazepines are those used for the drug therapy of anxiety disorders. Anti-depressant (mood-elevating agents) and antimanic (mood-stabilizing drugs) particularly Lithium salts and certain anticonvulsants and are used to treat affective or mood disorders and relative conditions. Antipsychotic or neuroleptic drugs are those which are used to treat very severe psychiatric illness the psychosis and mania. They have beneficial effect on mood and thought but many standard neuroleptic agents carrying the risk of producing characteristic side effects that mimic neuroleptic diseases, whereas modern antipsychotics are associated with weight gain and adverse metabolic effects such as diabetes.

KEY WORDS: Antipsychotic, disorders.

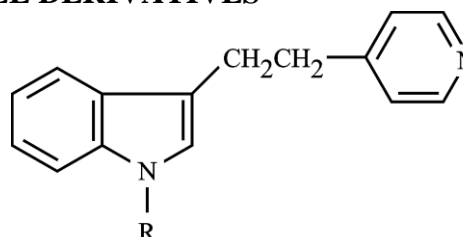
INTRODUCTION

Psychotropic drugs are the heterogenous group of compounds like indoles (oxypertine, indolyethylpyridines), phenothiazines (chlorpromazine, fluphenazine) dibenzoxazepine (loxapine succinate), dibenzothiazepine (quetiapine fumarate), benzodiazepines (olanzapine, clozapine) etc. These drugs possess diverse mechanism of actions the most widely used mechanism of action of this class of drugs is to antagonize dopamine D₂ receptors (typical antipsychotic drugs) or to antagonize dopamine D₁, D₃, D₄ and D₅ receptors

INDOLE DERIVATIVES

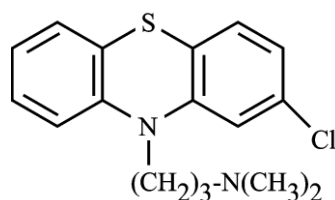


Oxypertine

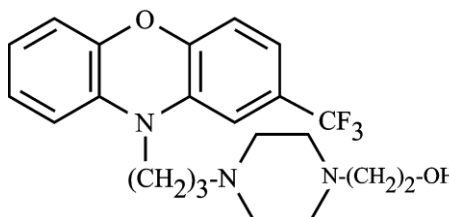


Indolyethylpyridines

Phenothiazine derivatives



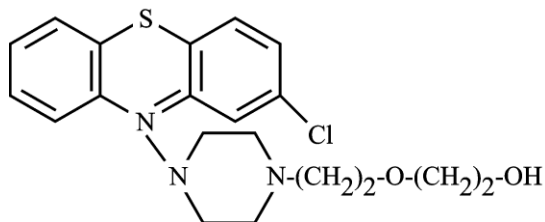
Chlorpromazine



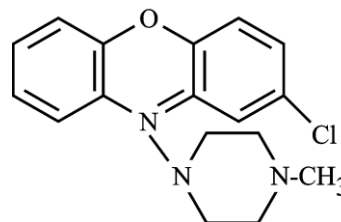
Fluphenazine

Dibenzothiazepine derivatives

Dibenzoxazepine derivatives

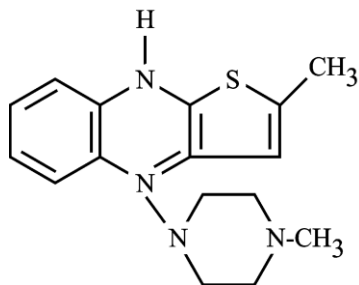


Quetiapine fumarate

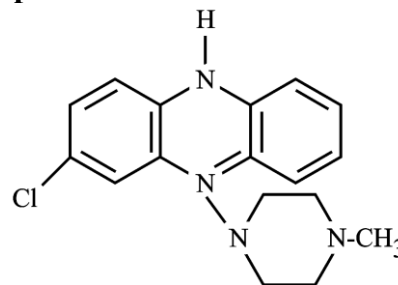


Loxapine succinate

Dibenzodiazepine derivatives



Olanzapine

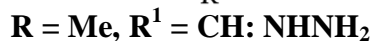
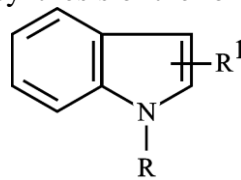


Clozapine

In addition to these known typical and atypical antipsychotic drugs, a larger number of derivatives of different heterocyclic moieties like indole, phenothiazine, benzothiazepine, benzoxazepine, quinazolinone etc. have been synthesized and screened for their psychotropic or antipsychotic activity by different scientists, which are described as follows-

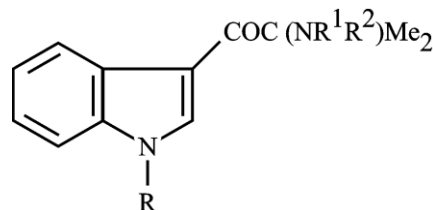
INDOLE DERIVATIVES

Indole derivatives have been found to be biologically versatile compounds which possess potent antihypertensive, anticonvulsant, anti-pyretic, anti-inflammatory, hypnotic and antipsychotic properties. In addition many indole derivatives notably molindone, oxypertin and inolyethylpyridines are well known for their neuroleptic or antipsychotic action. Moreover, several scientists have also elucidated that the modification (at position 2 or 3) in the indole nucleus by different heterocyclic moieties yields the potent antipsychotic agents which is proved by the synthesis of the following compounds by various scientists



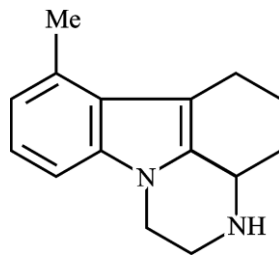
(I)

Some indolyl-2-amino-2-methyl propanones (II) have reported as useful psychotropic agents (Parcel et al., 1981)



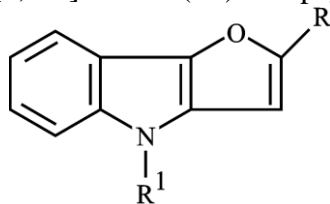
(II)

Mashkovskii et al.(1983) have reported psychotropic 1, 10-trimethylene-8-methyl-1,2,3,4-tetrahydropyrazine [1,2-a]indole (III).



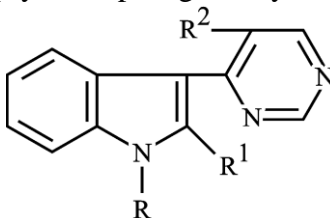
(III)

Yoshina et al. (1985) have reported furo [3,2-b]indoles (IV) as a psychotropic agents.



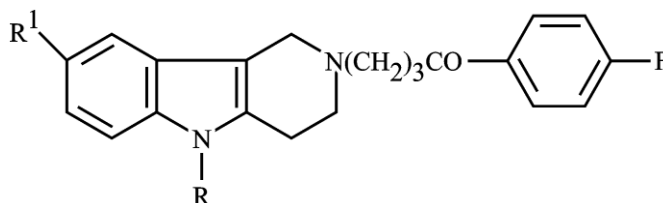
R = H, halo, alkyl etc., R¹ = H, alkyl
(IV)

Pyrimidinylindoles (V) have reported as psychotropic agents by Biere et al. (1986).



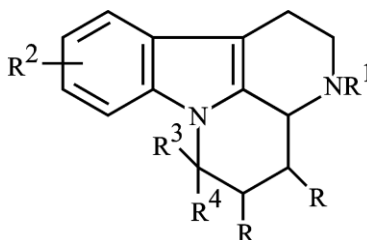
R = H, Me, (CH₂)₃ NEt₂, R¹ = H, NH₂, Me, R³ = H, OH, OMe
(V)

2,3,4,4a,5,9b-Hexahydro-1H-pyrido[4,3-b]indole (VI) derivatives exhibited prominent psychotropic activity (Nagai et al., 1987).



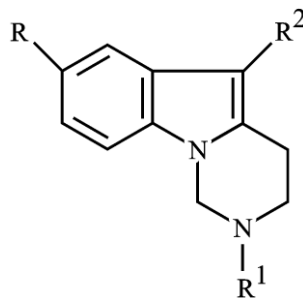
R, R¹ = Me, Et
(VI)

Indolo [3,2,1-de] [1,5] naphthyridine derivatives (VII) showed psychotropic and antianoxic properties as reported by Koletar et al. (1988).



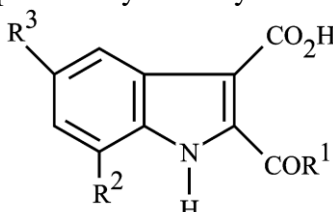
**R = H, CO₂Me, CONMe, R¹ = Me, Bz, NCCH₂CH₂,
R² = H, 9-or 10-Me,F,Cl, R³ = Me; R⁴ = OH; R⁵ = H**
(VII)

2-Substituted-2,3,4,5-tetrahydro-1H-pyrido[4,5-b]indole derivatives (VIII) exhibited psychotropic activity as reported by Nagai et al. (1990).



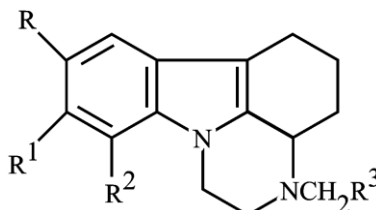
R= H, Cl, Me, R¹= Me, CH₂, R²= Ph CH₂
(VIII)

Zhungietu et al. (1990) reported neurotropic activity in 2-acylindole-3-carboxylic acids (IX).



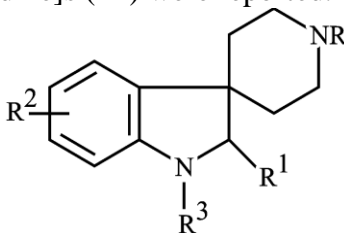
R¹ = Ph, p- Cl C₆H₄, p- BrC₆H₄, R² = H, me, R³ = H, Br, MeO, Cl
(IX)

Grinev et al. (1991) reported the marked psychotropic activity in 1, 10-trimethylene-1,2,3,4-tetrahydropyrazino[1,2-a]indoles (X).



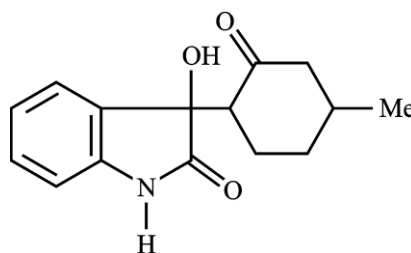
R= Me, Cl, Br, H, R1= H, Cl, R2= H, Cl, R3= Me, Et, Pr
(X)

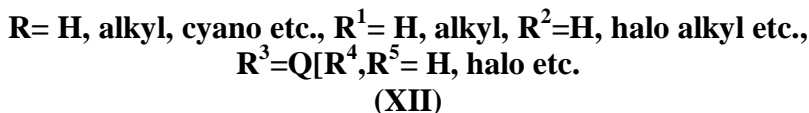
Anticonvulsant spiro[indoline-3,4'-piperidine]s (XI) were reported. (Ong & profil, 1992).



R= H, alkyl, cyano etc, R¹= H, alkyl, R²= H, halo alkyl etc,
R³= Q[R₄, R₅= H, halo etc
(XI)

3-Hydroxy indoles (XII) as potential anticonvulsants were reported by pojouhesh et al. (1993).





1-Phenyl-2-(1H,3H)-indolones (XIII) as psychotherapeutic agents have been reported by Howard & Sarges (1994).

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