Vol 2 | Issue 1 | Jan –Jun 2011 | 22-25. **Print ISSN – 2229 7502**

Research Article

SYNTHESIS, CHARACTERSATION, PHARMACOLOGICAL SCREENING ANTIMICROBIAL ACTIVITY OF 3-METHYL 1, 2-PHENYL (3-4-DIHYDROXY) 6-PHENYL PIPERIDINE-4-ONE

A. Senthil*[1], P. Suresh Kumar[1], CH. Narasimha Raju .BH[1], S. Mohideen[1], S. Navaneetha Krishnan[1]

[1.] Dept of Pharmaceutics, Browns College of Pharmacy, Khammam, AP.

ABSTRACT

The present study involves the synthesis, characterization, pharmacological and antimicrobial studies of 3-methyl 2 phenyl (3,4-hydroxy) 6-phenyl piperidine 4-one.This compound was prepared by Balial etal method. The synthesis compound was purified by crystallization using ethanol. The structure of the synthesized compound was assigned on the basis of the spectral data. IR and NMR showed the expected absorption frequencies and signals of this compound. Mass spectrum obtained different fragments and mechanism have been offered to explain these fragments. The antibacterial and antifungal activity of synthesized compound was studied by drug diffusion method and disc plate method. The compound did not show any antibacterial and antifungal activities against the organism mentioned. Local anesthetic activity of this compound carried out by infiltration anesthesia method it showed comparable activity with that of standard drug.

Key Words: Antimicrobial Activity, Antifungal, Diffusion Method, Disc Plate Method.

INTRODUCTION

The present study involves the synthesis, characterization pharmacological screening and antimicrobial activity of 3-methyl 2 phenyl (3,4-hydroxy) 6-phenyl piperidine 4-one.It is a potent antibacterial drug and shoe broad spectrum activity against various gram positive and negative organisms. A revolution in the synthesis of substituted 4-piperidone was created by Noller&Baliah [1] they prepared substituted piperidones by heating a mixture of ketone, aldehyde and ammonium acetate in acetic acid in the ratio of 1:2:1. Isaiah & co workers [2] reported that 2,6-bis(2-methoxy-phenyl)3-5-dimethyl 4-piperidone HCL.Bochringer & Soehne [3] prepared 1,2,6-trisubstituted-4-piperidones. Found to posses tranqulizer activity. Choderal *et al* [4]. Ebersbery & Haller synthesized various substituted cis 2-6-diphenyl-3-methyl-4-piperidinols by the reduction of 4-piperidones [5]. Tempidone had a moderately depressant effect [6] and has hypotensive effect, Lentral nervous system depressive effect [7] and analgesic activity [8]. Af.Ekanstan prepare piperidine dedicative and showed infiltrations anaesthetic activity comparable to that lidocaine mobio et al studied the activities of 2,3,6-triaryl 4-oxopiperidines showed bactericidal, fungicidal and herbicidal activity [9] and also N-substituted piperidine derivatives show antidepressant and nervous system stimulant activities as per literature review. The method of Woller & Baliah [1] was followed synthesize this compound and experimental studies, melting point by open capillary tubes, IR spedtra, NMR spectra showed the expected absorption frequencies and signals of this compound . Mass spectrum show different fragments. The antibacterial antifungal activity compound were studied by drug diffusion method 8 disc plate method and local anaesthetic activity was carried out by wheal preparation in Guinea pig showed comparable activity with that of standard drug lignocaine hydrochloride.

MATERIALS AND METHODS

Materials

All the solvent and reagents used for the study were of analytical grade procured from

*Corresponding Author **A. Senthil** E-Mail: senthil_ac12@yahoo.co.in

institution and were purified by standard methods.

Methods

1. Characterization

Melting points of the synthesized compound was taken in open capillary tubes.

IR Spectra was recorded on Win-Bomman B-104 IR spectrophotometer.

NMR spectra were taken in deuterated chloroform on a DPx-200 NMR spectrophotometer using TMS as internal standard.

Mass spectra was recorded on Finnegan mat 8230 spectrophotometer.

Thin layer chromatography was performed using plates coated with silica**.gel fi,R of** 0.25 ,mm thickness Carbon tetra chloride and petroleum ether [4:1] **"Used as** mobile phase. Spots were visualized in the Iodine chamber and **'U.V fight chamber.**

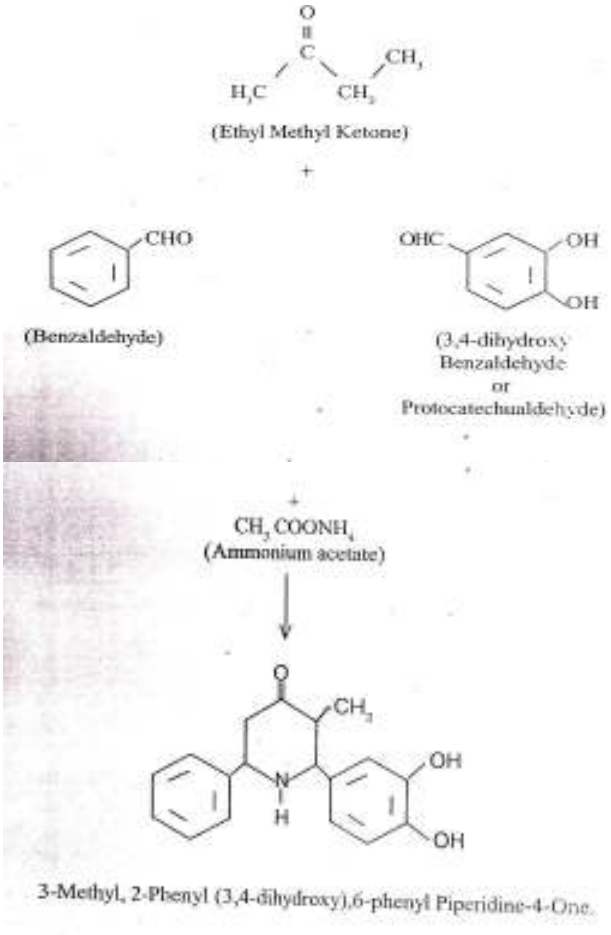
2. Method

2.1 Synthetic procedure

The method of Noller and Baliah [1] was followed to synthesize this compound. A mixture of ethyl methyl ketone (9ml, 0.lVl); dry ammonium acetate (7.7 gm. 0.1M); benzaldehyde (10.5ml, 0.1 M) & Protocatechualdehyde (13.8 gm, 0.1M) was mixed with ethanol (30ml) and heated to simmering carefully. The flask was kept at room temperature for 12 hours. Diethyl ether (50ml) was added followed by concentrated hydrochloric acid (30 ml) and cooled in ice water. The precipitate was filtered, washed with ethanol-ether mixture (1:5) and transferred to an one litre beaker. The precipitate was suspended in acetone and basified with strong ammonia Solution. The base liberated out on the dilution with excess of water. It was filtered, washed repeatedly with water and dried. The crude piperidin-4-one was recrystallised from ethanol. The yield was 72% and the pure sample was melted at 73°C Retardation factor (R_f): 0.58.

2.2 Synthetic schemes

Synthetic Scheme of 3-methyl, 2-Phenyl (3-4-dihydroxy) 6-Phenyl Piperidine- 4-one.



Pharmacological activity

1. Local anaesthetic activity:

Wheal preparation method .Guinea pigs weighing between 300grams to 350grams shave the hair. They were divided into four groups of two animals in each group

Group I: solvent control (propylene glycol).Group II: 0.2ml (1% lignocaine HCl) standard. Group III: 1% concentration of drug(3-methyl,2-phenyl(3-4-di hydroxy) 6-phenyl piperidin-4-one). Group IV: 2% concentration of drug (3-methyl, 2-phenyl(3-4-di hydroxy) 6-phenyl piperidin-4-one). Now the drug substance is given intradermally. After 5minutes the sensitivity of the area was tested by pricking with a needle, six times. Lightly on the skin at site of injection. Failure to the twitch upon pricking was recorded as negative response. The test was repeated at five intervals for a period of 20 minutes after 30,45,60.90 and 120minutes. Local anaesthetics are drugs, that block conduction of impulses in nerves, when applied locally to nerve tissue in appropriate concentrations. Thev act on any part of nervous system and on every type of nerve fibre [10].

The compound of 3-methyl 2-phenyl (3,4-dihydroxy) 6-phenyI, piperdine 4-one, at 1% and 2% concentrations, and the standard lignocaine hydrochloride of 1% concentration, showed the onset of action of 5 minutes. The compound was found to sustain activity upto 2 hrs of duration. The results of the study are mentioned in Table No-1.

The compound at the concentration of 1% showed comparable local anaesthetic activity, with that of standard Lignocaine hydrochloride. The local anaesthetic activity increased with an increase in the concentration of 2%, and was found to possess slightly greater Local anaesthetic action, than that of standard.

2. Antibacterial activity

Disc diffusion method

Prepared the Bacterial Subculture the test , organism was inoculated in 20ml of nutrient broth and incubated at 37°C for 18-20 hrs.and muller,Hinto agar (m-173) media was poured into sterile Petri dishes and solidified the plates were dried at 37°. for 30mts. The subculture was diluted

Disc diffusion method

The synthesized compound at different, concentrations of 1 mg/ml, 2mg/ml and 5 mg/ml was prepared by dissolving them separately in DMSO (Dimethyl sulfoxide) to form the test solutions. Sterile discs 5mm in diameter (made from Whatman's filter paper) were dipped in the above test solution. Sterile saline by using sterile cotton swab dipped into broth culture and swabbed in three directions and inoculated the plates. The above prepared disc was placed in the inoculated plate along with solvent control and standard.

Antifungal Activity:

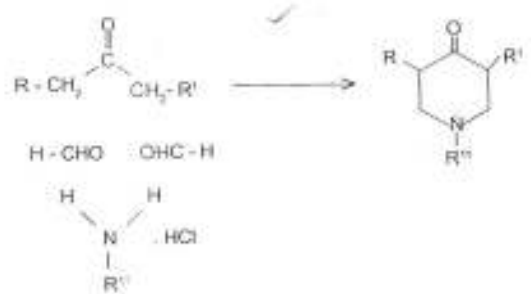
The activity was studied by the disc plate method against the organisms Candida albicans, Candida tropicals, and *Aspergillus niger* the test organism was inoculated in 20ml of nutrient agar slopes and incubated at 37°c for 18-20 hrs. The preparation of disc containing compound of 5,10mg/ml concentration were prepared by dissolving them in DMSO to form the test solution. The discs were dipped in the test solution placed in the inoculated plate along with solvent control. The plate was incubating 24 hrs at 37°c and observes the zone of inhibition.

RESULT AND DISCUSSION:

Various Piperidin -4-one derivatives were synthesized by Mannich reaction. A number of 2,6-diaryl piperidin-4 one have been synthesized by Baliah *et al*. [10][34]. They were obtained by the condensation of Dialkyl ketone, aromatic aldehyde, and Ammonium acetate.

The condensation is acetic acid medium, Provide a slightly coloured Product, where as the condensation in ethanol, Provide a colourless Product. In this synthetic procedure, 4-piperidones are obtained in very good yield

Methods are also available for synthesising simple 4-Piperidones without aryl group. In this case, reaction between an aliphatic ketone, 35% formaldehyde Solution and ammonium acetate methyl or dimethyl amine hydrochloride yield.



The synthesised 4-Piperidone were characterised through IR, PMR, and Mass spectra. The synthesised 4-piperidone, are expected to show Characterstic absorption bands in IR Spectrum for N-H, C=0, and C=C bonds.

Lyle and Lyle [27] observed that in 1-methyl, 2,6-Diphenyl, 4-piperidone, the C=0 absorption band was noted at 1720cm[1], 2,2,6,6-tetra methyl-4- Piperidone show the carbonyl stretching absorption in the 1700-1720 cm'[1] region, the N-H stretching frequency was observed at 2900 cm"[1], and 3300 cm*[1], and the C-H, bending Vibration in the region 960-600 cm"

IR. Spectral data (KBr Pellets) Wave number in Cm

3034 - 3086 —> Aromatic C-H Stretching
2935 - 2975 —> Aliphatic C-H Stretching
699 - 767 —> Aromatic C-H bonding
1417 -1458 —> Aliphatic C-H bonding
1407 (s) —> C=o Stretching,
3312—> Phonetic - OH, - NH Stretching (Both are merged)
335 – 376 —> Phenolic OH Bonding
1617(W) —> N-H- bonding
1458- 1617 —» Ar - C=C Stretching,
1276 —> Phenolic C-0 Stretching.
For the 3-MethylDiphenyl -4-Piperidone.

I) Local Anaesthetic Activity:

Loca anaesthetics are drugs that block conduction of impulses in nerves, when applied locally to nerve tissue in appropriate concentrations. They act on any part of nervous system and on every type of nerve fibre.

The compound of 3-methyl 2-phenyl (3,4-dihydroxy) 6-Phenyl, piperidine 4-one, at 1% concentration,showed the onset of action of 5 minutes. The compound was to sustain activity upto 2 hrs of duration. The results of the study are mentioned in table No-1.

The compound at the concentration of 1% showed local anaesthetic activity, with that of standard lignocaine hydrochloride. The local anaesthetic activity increased with an increase in the concentration of 2% and was found to posses slightly greater local anaesthetic action, than that of standard.

Antibacterial Studies:

Mobio et al reported that 2, 3,6-triaryl-4-one piperidine posses antibacterial activity. The test result indicated no significant antibacterial activity for compound at the different concentrations tested against the organisms mentioned.

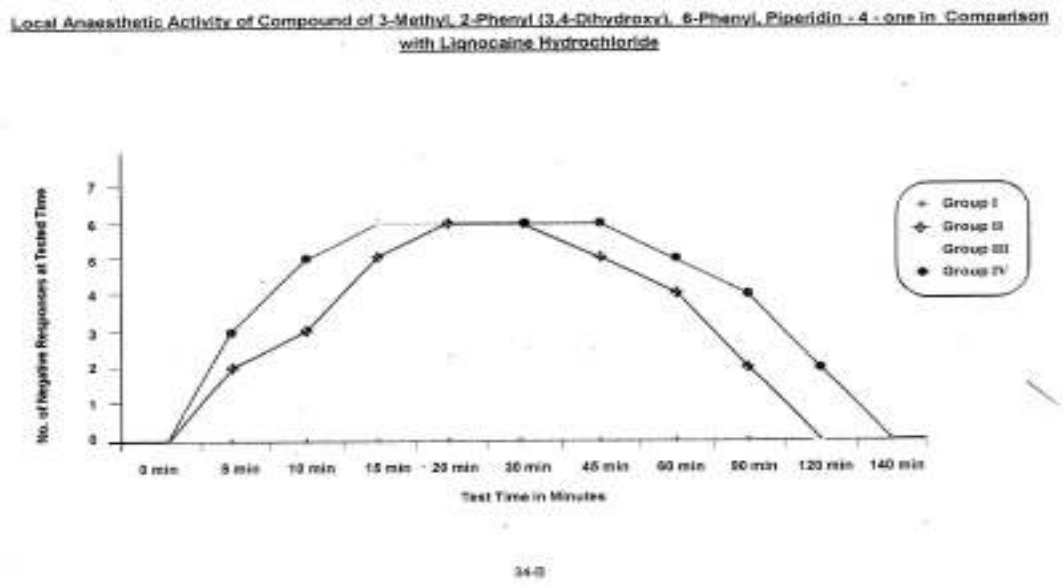
Antifungal Studies:

The compound at different concentrations of 5mg/ml and 10mg/ml, exhibited the antifungal activity against the organisms of Candida albicans, Candida tropical and aspergillus niger.

Local Anaesthetic activity of compound of 3-methyl,2-Phenyl (3,4-Dihydroxy),6 Phenyl,Piperidin-4-one in comparison with Lignocaine by hydrochloride

"GUINEA PIG WHEAL METHODS" Route of administration: Intradermal

Groups	Drugs	Concentration Injected	Time in Minutes										Total Number of Negative response out of 66
			0	5	10	15	20	30	45	60	90	120	140	
Group-I	Control	Propylene Glycol	0/6	0/6	0/6	0/6	0/6	0/6	0/6	0/6	0/6	0/6	0/6	0
Group-II	Lignocaine Hydrochloride (Standard)	1%	0/6	2/6	3/6	5/6	6/6	6/6	5/6	4/6	2/6	0/6	0/6	33
Group-III	Compound	1%	0/6	2/6	4/6	6/6	6/6	5/6	4/6	3/6	2/6	0/6	0/6	32
Group-IV	Compound	2%	0/6	3/6	5/6	6/6	6/6	6/6	6/6	5/6	4/6	2/6	0/6	43



REFERENCES

1. Noller CR and Baliah V. *J.Am. Chem.Soc,* 70, 1948, 3853.
2. Iswariah V and Venkatasubbu VS. *Current Sci*(India), 21, 1952, 248.
3. Baliah V and Gopalakrishnan V. *J. Indian Chem. Soc*, 31(3), 1954, 250.
4. Sivasubramanian S, Sundaravadivelu M and Arumugam N. *Indian J.Chem***.,** 20(B), 1981, 878.
5. Bochringer CF and Shoehne GMBH. *Brit.Pat*. 866, 1961, 488.
6. Ebersberg J and Haller, Rolf Arch.Pharm.(Weinheim), 302(4), 1969, 248.
7. Zhelyazhov H, Bikova N, Krusteva L, Deleva L, Nikolova M, Sheikova Zh, Nacheva M, St.Vankov and Ilarionov I. *Tr.NanchorizsIed. Khim-Farm. Inst*., 7, 1972, 23.
8. Nikolov M, Stefanova D and Chardanov D. *Act. Nerv. Super.*, 16(4), 1974, 264.
9. Andreeva LV. *Persperktivy Nauch.Minsu*., 48, 1978, 52.
10. Cruick Shank R, Dugid JP, Marmion BP and Swain, RHA. Medical Microbiology**,** 12th Edition, Vol-II, Churchill Livingstone, New york, 1975, 196-201.