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Antimicrobial and Antioxidant Activities of 3-Methyl-2-Aryl-*trans*-decahydroquinolin-4-ols

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Two sets of epimers of the system 3-methyl-2-aryl-*trans*-decahydroquinolin-4-ols were synthesized by known methods and screened for antimicrobial and antioxidant activity. The compound 3-methyl-2-p-chlorophenyl-*trans*-decahydroquinolin-4-ol exhibited antifungal activity against *Aspergillus niger* and antibacterial activity against *Styphylococcus aureus* and *Proteus vulgaris*.

Key words: Decahydroquinolin-4-ols, Antimicrobial activity, Antioxidant activity.

Nitrogen containing compounds like quinolines, piperidones and substituted piperidones, quinolones and their derivatives exhibited a broad range of biological activity (Aznar *et al.,* 1985). These may possess analgesic, anti-inflammatory, antimicrobial and antioxidant activity. Oliphant *et al* (2002) in his review identified that most of the quinolones were active against gram negative bacteria and also identified that some of the quinolones developed have been reported to be active against gram positive bacteria. In view of the observed activities of nitrogen containing compounds the present investigation was taken up. For this purpose two sets of epimers 3-methyl-2-aryl-*trans*-decahydroquinolin-4-ols were synthesized and the stereochemistry of the compounds was confirmed with the data reported previously by using computational approach (Hari babu *et al.,* 2007) and proton NMR spectroscopy (Hari babu *et al.,* 2008).

MATERIAL AND METHODS

In the present investigation the compounds (Fig. 1) 3-methyl-2-p-tolyl-*trans*-decahydroquinolin-4-ol (equatorial) (compound I), 3-methyl-2-p-tolyl-*trans*-decahydroquinolin-4-ol (axial) (compound II); 3-methyl-2-p-chlorophenyl-*trans*-decahydroquinolin-4-ol (equatorial) (compound III), and 3-methyl-2-p-chlorophenyl-*trans*-decahydroquinolin-4-ol (axial) (compound IV) were prepared by the methods developed by Baliah and Natarajan(1989), which involves

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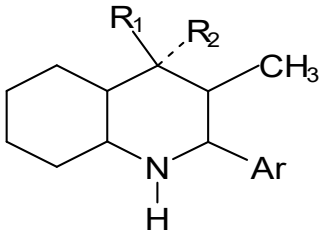
synthesis of required ketones followed by subjecting the ketones to sodium n-butanol reduction and Meerwein-Ponndorf-Verley(M.P.V) reduction. Further, the compounds were screened for antioxidant and antimicrobial activity.

The antimicrobial activity was determined with a filter paper disc method (Cappuccino and Sherman, 2004). The test microorganisms include *Aspergillus niger*, *Candida albicans* (MTCC 183), *Escherichia coli* (MTCC 40), *Pseudomonas aeruginosa* (MTCC 424), *Staphylococcus aureus* (MTCC 96), *Bacillus cereus* (MTCC 430). The suspension of test bacteria (200 ml) was added to 100 ml of sterilized nutrient agar medium and then poured into sterile Petri plates. The plates were allowed to solidify. In the case of antifungal assay, fungal spore suspension was spreaded on to solidified Czapek-Dox agar medium. Sterilized paper discs were placed on nutrient agar medium and Czapek-Dox agar medium, which were seeded with the test organisms. To the discs 50ppm compounds were added. Controls were maintained with filter paper discs with out compound.

The antioxidant activity of the compounds was carried out by two different methods, namely Superoxide free radical scavenging activity and DPPH (1,1-diphenyl-2-picryl-hydrazyl) radical scavenging activity.



Compound I: R1=H, R2=OH, Ar= p-CH3C6H4. 3-methyl-2-p-tolyl-trans-decahydroquinolin-4-ol (equatorial)
Compound II : R1 = OH, R2 = H, Ar = p-CH3C6H4. 3-methyl-2-p-tolyl-trans-decahydroquinolin-4-ol (axial)
Compound III. R1 = H, R2 = OH, Ar = p-Cl-C6H4. 3-methyl-2-p-chlorophenyl-trans-decahydroquinolin-4-ol (equatorial)
Compound IV. R1 = OH, R2 = H, Ar = p-Cl-C6H4. 3-methyl-2-p-chlorophenyl-trans-decahydroquinolin-4-ol (axial)

Fig. 1. 3-methyl-2-aryl-*trans*-decahydroquinolin-4-ols

Superoxide free radical scavenging activity

Superoxide radicals were generated in-vitro by non-enzymatic system and determined spectrophotometrically by following the Nitro Blue Tetrazolium (NBT) riboflavin photoreduction method of McCord and Fridovich (1969). The assay mixture contained EDTA (6.0µM), NaCN (3µg), riboflavin (2µM), NBT (50µM) and various concentrations of test substances in methanol and phosphate buffer (58mM, pH 7.8), in a final volume of 3mL. The tubes were shaken well and the absorbance was measured before and after illumination at 560nm. The percentage of inhibition of superoxide radical generation was measured by comparing the mean absorbance values of control and those of the test substances. The antioxidant activity of the compounds was expressed as the 50% inhibitory concentration (IC_{50}) that was measured from the plot drawn concentration (µg) verses percentage inhibition.

DPPH (1,1-diphenyl-2-picryl-hydrazyl) Radical scavenging activity

DPPH (1,1-diphenyl-2-picryl-hydrazyl)-radical scavenging activity was determined by the method described by Lamaison, *et al* (1991) based on the reduction of methanolic solution of the colored DPPH. IC_{50} values were obtained from the plot drawn concentration in µg verses percentage inhibition. The reaction mixture contained 1.0 x 10^{-4}mM methanolic solution of DPPH and various concentrations of test substances and kept in dark area for 50min. The absorbance of the samples was measured on a spectrometer at 517nm against a blank.

RESULTS AND DISCUSSION

Data on the antimicrobial spectrum of chloroform extracts of the compounds I-IV are presented in Table-1. All the compounds assayed in the present study were found to be inhibitory to gram positive bacteria like *Bacillus cereus*, *Bacillus subtilis* and *Staphylococcus aureus*. Gram negative bacteria like *Proteus vulgaris* and *Pseudomonas aeruginosa* and fungi include *Aspergillus niger* and *Candida albicans* were also found to be sensitive to the compounds. Among the four compounds, the compound IV was found to be highly active against all the test

microorganisms. The compounds I, II and III were showing almost equal similarity in antimicrobial activity against all the test microorganisms. *Staphylococcus aureus, Proteus vulgaris* and *Aspergillus niger* were highly sensitive to IV followed by *Bacillus cereus*, *P. aeruginosa*, *E. coli*, *B. subtilis* and *Candida albicans.*

The present study clearly revealed that the biological activity of the compounds mainly depends on the aryl ring at second position and the conformation of the hydroxyl group present in the position 4. Ramesh kumar *et al* (2003)reported that the compounds like 2-(4-methylphenyl)-3-methyl-6-(4-hydroxyphenyl)-piperidin-4-oxime and 2-(4-methoxyphenyl)-3-methyl-6-(4-chlorophenyl)-piperidin-4-oxime exhibited potent antifungal activity against *Aspergillus niger* and 2-(4-dimethyl-aminophenyl)-3-methyl-6-(4-chlorophenyl)-piperidin-4-oxime exhibited activity only against *Candida albicans*.

Typical heterocyclic compounds (Khanum *et al.,* 2003) such as pyrroles, furans and thiophenes substituted with various functional groups were proved to be antioxidants and thiazoles and pyrazines were reported as ineffective antioxidants. In the present study, the compounds exhibited negligible antioxidant activity at all the concentrations tested (Table 2 and 3). Among the four test compounds, compound III was found be showed good antioxidant activity. The present study clearly revealed that the biological activity of the compounds mainly depends on the aryl ring at second position and the conformation of the hydroxyl group present at the fourth position. The compound IV was found more promising antimicrobial compound.

Table 1. Antimicrobial activity of the compounds I, II, III and IV

Microorganism	(Diameter of inhibition zone (mm))			
	I	II	III	IV
Bacteria				
Bacillus cereus	6	10	3	16
Bacillus subtilis	5	8	3	10
Staphylococcus aureus	4	8	3	20
Proteus vulgaris	8	8	5	20
Pseudomonas aeruginosa	8	8	6	14
Escherichia coli	10	8	6	12
Fungi *Candida albicans*	-	6	-	8
Aspergillus niger	-	8	-	16

Table 2. Superoxide radical scavenging activity of 3-methyl-2-aryl-*trans*-decahydroquinolin-4-ols

Test substance	% of Inhibitionat 100 µg	IC_{50} (in µg)
Compound I	13.3	>100
Compound II	6.79	>100
Compound III	18.8	>100
Compound IV	3.34	>100
Vitamin-C	97.52	150
BHA	52.18	174

*BHA - Butylated Hydroxy Anisole

Table 3. DPPH-radical scavenging activity of 3-methyl-2-aryl-trans- decahydroquinolin-4-ols

Test substance	% of Inhibitionat 100 µg	IC_{50} (in µg)
Compound I	4.9	>100
Compound II	7.35	>100
Compound III	22.81	>100
Compound IV	4.39	>100
Vitamin-C	77.3	6.1
BHA	88.09	3.2

*BHA - Butylated Hydroxy Anisole

REFERENCES

1. Aznar, J., Maria C. Caballero, Mariac Lozano, Constantino Demiguel Jose C. Palomares, Evelio J. Perea, Activities of new quinoline derivatives against genital pathogens. *Antimicrobial agents and chemotherapy*, 1985; **27**(1): 76-78.
2. Baliah V and Natarajan A, Conformations of some decahydroquinolin-4-ols: Study by kinetics of chromic acid oxidation, *Indian. J. Chem.*, 1989; **28A**, 609-611.
3. Cappuccino, J.G. and Sherman, N. (2004). Microbiology, a laboratory manual. Pearson Education, Inc., New Delhi, pp. 282-283.
4. Hari Babu, B. and Satyanarayana, P. V. V., Conformational analysis of 2-aryl-*trans*-decahydroquinolin-4-ols. ii. A kinetic and computational approach. *Oxidation Communications* (Scientific Bulgarian Communications), 2007; **30**(1): 8–18.
5. Hari Babu, B., and Satyanarayana, P. V. V., Configuration and Conformational Analysis of some substituted 2-aryl-*trans*-decahydroquinolin-4-ols by Proton NMR Spectroscopy. *Int. J. Pure and applied Chem.* (2008); **3**(1): 57-63.
6. Lamaison, J.L., Ptitjean-Freytet, C. and Carnet, A., DPPH scavenging activity. *Pharma Acta Helv.***,** 1991; **66**: 185
7. McCord, J.M. and Fridovich, I. Superoxide dismutase: an enzymic function for erythrocuprein (hemocuprein). *J. Biol. Chem*., 1969; **244**: 6049-6055.
8. Oliphant, C.M. Quinolones: A Comprehensive Review, American Family Physician, 2002; **65**(3): 455-464.
9. Ramesh Kumar, Anantharamanveena, Raju Ilavarasan, Mandaleeswaran Adiraj, Pitchaimuthu Shanmugapandiyan, Seshaiah Krishnan Sridhar, Synthesis and Biological Activities of 2,6-Diaryl-3-methyl-4-piperidone Derivatives**.** *Biol. Pharma. Bull*., 2003; **26**(2): 188-193.
10. S.A Khanum, Sheena shashikanth, Belagur S. Sudha, A Facile Synthesis and Antimicrobial Activity of 3-(2-Aroylaryloxy)methyl-5-Mercapto-4-Phenyl- 4H-1,2,4-Triazole and 2-(2-Aroylaryloxy)methyl- 5-N-Phenylamino-1,3,4-Thiadiazole Analogues. *Science Asia*, 2003; **29:** 383-392.