WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 12, Issue 18, 770-776. Research Article ISSN 2277– 7105

CYTOTOXICITY STUDY OF SOME INDOLE DERIVATIVES

[1]*Aswani Purandharan, [2]Jithamol K.P., [3]Sonu Jacob and [4]Kavitha S.

[1,2]Assistant Professor, Department of Pharmaceutical Chemistry and Analysis, Chemists College of Pharmaceutical Sciences and Research, Puthencruz, Ernakulam, Kerala.

[3]Associate Professor, Department of Pharmaceutical Chemistry and Analysis, Chemists College of Pharmaceutical Sciences and Research, Puthencruz, Ernakulam, Kerala.

[4]Assistant Professor, Department of Pharmaceutical Chemistry, KMP College of Pharmacy, Perumbavoor, Kerala.

Article Received on
26 August 2023,

Revised on 16 Sept. 2023,
Accepted on 06 Oct. 2023

DOI: 10. 20959/wjpr202318-29928

***Corresponding Author**
Aswani Purandharan
Assistant Professor, Department of Pharmaceutical Chemistry and Analysis, Chemists College of Pharmaceutical Sciences and Research, Puthencruz, Ernakulam, Kerala.

ABSTRACT

Seven indole derivatives were synthesized for the interest of studying biological activity especially for cytotoxicity. The cytotoxicity of some indole derivatives was studied by the brine shrimp lethality bioassay. It was observed that all the indole derivatives showed potential cytotoxicity against brine shrimp nauplii.

KEYWORDS: Indole, Cytotoxicity, Brine shrimp.

INTRODUCTION

Indoles are one of the most important nitrogen containing bicyclic heterocyclic molecules, found extensively in biological system which play vital role in biochemical process. The indole nucleus is an important structure in numerous natural or synthetic alkaloids, and in medicinal chemistry.[2]

The research on indole began in the mid nineteenth century with the investigations of indigo. Since ancient times indigo has been used as a dye. In 1841, this dye was oxidized to isatin and in 1866, isatin was reduced to oxindole. The zinc dust distillation of oxindole gives indole. The indole was first prepared synthetically by Adolf Von Baeyer in 1866. The revival of the research indole chemistry took place in the 1930, when it was discovered that many alkaloids contain the indole ring system. The research was further stimulated by the discovery of the biological activities of indoles. It possess interesting biological activities like

antimicrobial, antiviral, anti-inflammatory, anticancer, antidiabetic, antioxidant, antidepressant and anticonvulsant activities.[4]

This work has been carried out from the synthetic point of view along with their biological property especially cytotoxicity by brine shrimp lethality bioassay.[1]

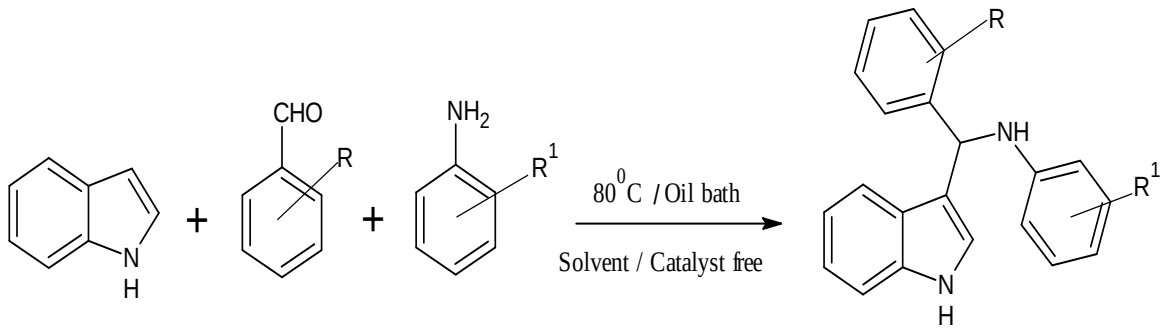
EXPERIMENTAL SECTION

Materials and Methods

All the chemicals were purchased from Merck Specialities Pvt. Limited, Mumbai, Himedia Laboratories Pvt. Limited Mumbai.

General procedure for the synthesis of substituted indoles

A mixture of aromatic amine (1mmol) and aromatic aldehyde (1mmol) was stirred in a preheated oil bath at 80^0C. Indole (1mmol) was added after 10minutes and the mixture was heated for the appropriate amount of time. The progress of the reaction was monitored by thin layer chromatography. After completion, the reaction mixture was cooled to room temperature and ethanol was added. The total solution was poured in to water (50ml). The colourless precipitate thus formed was filtered. The filtered product was thoroughly washed with water and dried in a watch glass. The air dried crude product was crystallized with suitable solvent.[3]

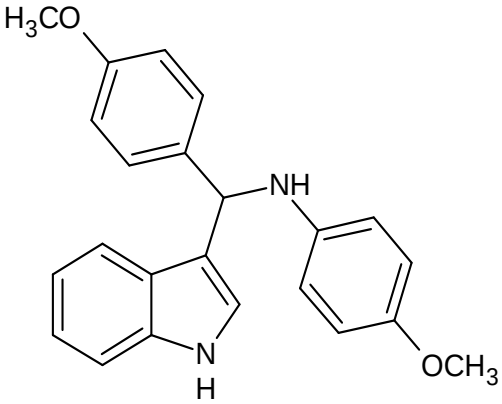


Indole | Aromatic Aldehyde | Aromatic Amine | 3-substituted indole

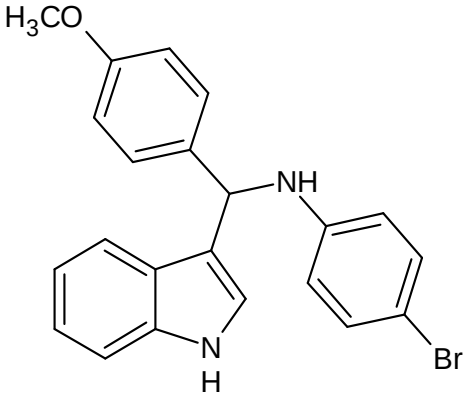
R = Benzaldehyde, Chloro benzalehyde, Anisaldehyde

R^1 = Anisidine, 4- Bromoaniline, 4-Nitroaniline, 2, 4 Dinitroaniline

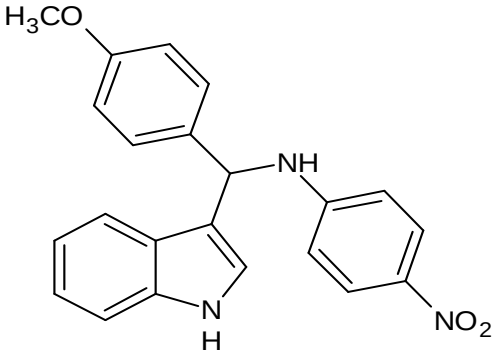
Substituted compounds



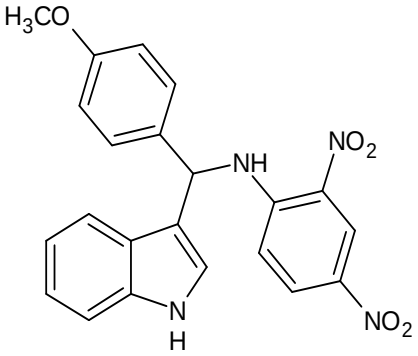
IAA$_4$



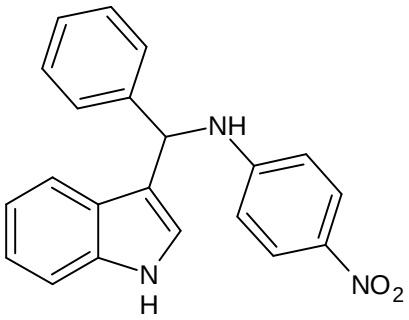
IBA$_4$



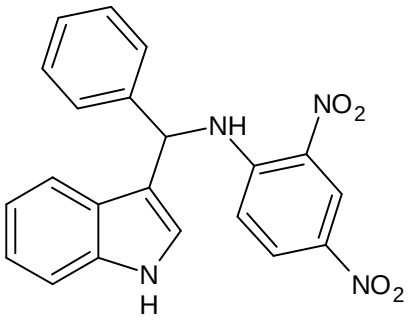
INA$_4$



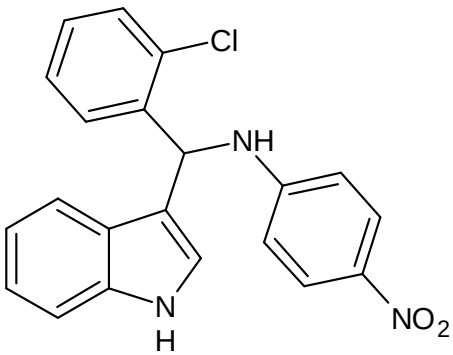
INA$_{2,4}$



INB$_4$



INB$_{2,4}$



INC$_4$

BIOLOGICAL EVALUATION

Cytotoxicity study

The cytotoxicity of the synthesized compounds was studied by brine shrimp lethality bioassay.[5]

Test animal

Brine shrimps (Artemia Salina) were used as test animal for the investigation of cytotoxicity.

Hatching and maintenance of brine shrimp

The preferred condition for brine shrimp (temperature 28-30°C), was established by mixing sodium chloride salts in water. After obtaining the desired condition, about one teaspoon of brine shrimp eggs was added to the beaker. After 40 hour hatching aggregated brine shrimp nauplii were collected and applied for testing.[6]

Preparation of test sample

For the cytotoxicity study, dimethyl sulphoxide (DMSO) was used as a solvent and the mortality of brine shrimp nauplii in this DMSO solution was almost zero. Different concentrations (5, 10, 25, 50 µg/ml) of each test samples were prepared with DMSO. Then 10-12 brine shrimp nauplii were transferred to each test tube using micropipette.[7]

Counting of nauplii

The numbers of survived nauplii in each test tube were counted. The percentage of mortality of brine shrimp was calculated for each sample that gives different mortality for different concentrations.[10] An approximate linear correlation was observed when logarithm of concentration was plotted against percentage of mortality and the values of IC50 were calculated for each sample. The IC50 represents the concentration of a compound, which will kill, or inactive 50 percent of the test animal. IC50 is inversely proportional to the toxicity of a compound, i.e. the lower the IC50 the higher the toxicity.[8,9]

RESULT AND DISCUSSION

The preliminary cytotoxicity study of indole derivatives were carried out in brine shrimp lethality bioassay. All the synthesized compounds showed adequate cytotoxic effect. From the results of IC_{50} determination, all the concentration of compounds is safe up to 24hr, further the experiment was extended up to 48hr. The results shows that a IC_{50} values of IAA_4 IBA_4, INA_4, $INA_{2,4,}$ $INB_{4,}$ $INB_{2,4}$, INC_4 are1.3, 0.4, 1.2, 1.3, 1.4, 0.7, 0.9 log values

respectively. IC_{50} is inversely proportional to the toxicity of a compound, i.e. the lower the IC_{50} the higher the toxicity. The compound IBA_4 shows better cyctotoxicity compared to remaining all other compounds. $INB_{2,\ 4}$, INC_4 are moderately active. All the remaining compound shows lesser activity.

CONCLUSION

In conclusion we have described a simple, rapid and facile synthetic route for some indole derivatives. The purpose of the synthesis of such heterocyclic compounds was to determine cytotoxicity against brine shrimp. From the results it can be stated that structural modification of molecules led to alteration in bioactivity such as cytotoxicity. Substitution with halogen in the aromatic system resulted in greater cytotoxicity. From the results it can be stated that structural modification of molecules led to alteration in cytotoxicity, in future we can able to produce more potent drug with safer dose.

Table 1: Cytotoxic effect by brine shrimp assay.

SI no:	Groups	Concentration (µg/ml)	% mortality at 24hr	% moratality at 48hr
1.	CONTROL	0	0	10
2.	IAA_4	5 10 25 50	0 0 10 30	20 40 60 70
3.	IBA_4	5 10 25 50	0 60 80 100	85 90 95 100
4.	INA_4	5 10 25 50	0 0 0 20	30 40 60 80
5.	$INA_{2,4}$	5 10 25 50	0 0 40 70	20 30 60 90
6.	INB_4	5 10 25 50	0 0 20 60	20 30 50 100
7.	$INB_{2,4}$	5 10 25 50	25 40 45 65	50 80 90 100
		5	0	30

8.	INC_4	10 25 50	0 10 40	60 80 90

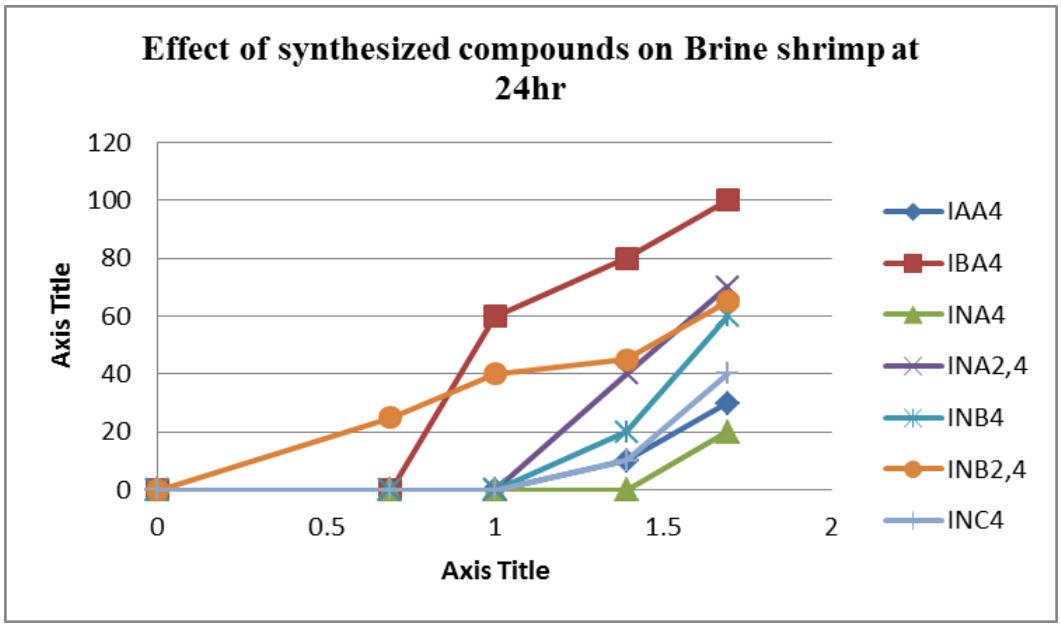


Figure 1: effect of synthesised compounds on brine shrimp at 24hr.

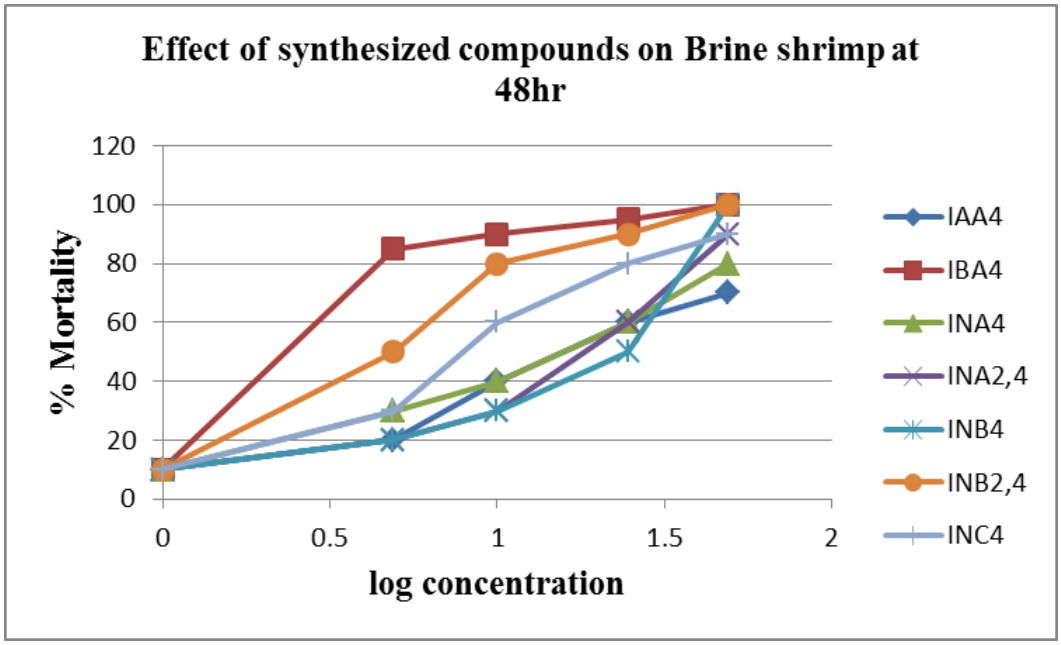


Figure 2: effect of synthesised compounds on brine shrimp at 48hr.

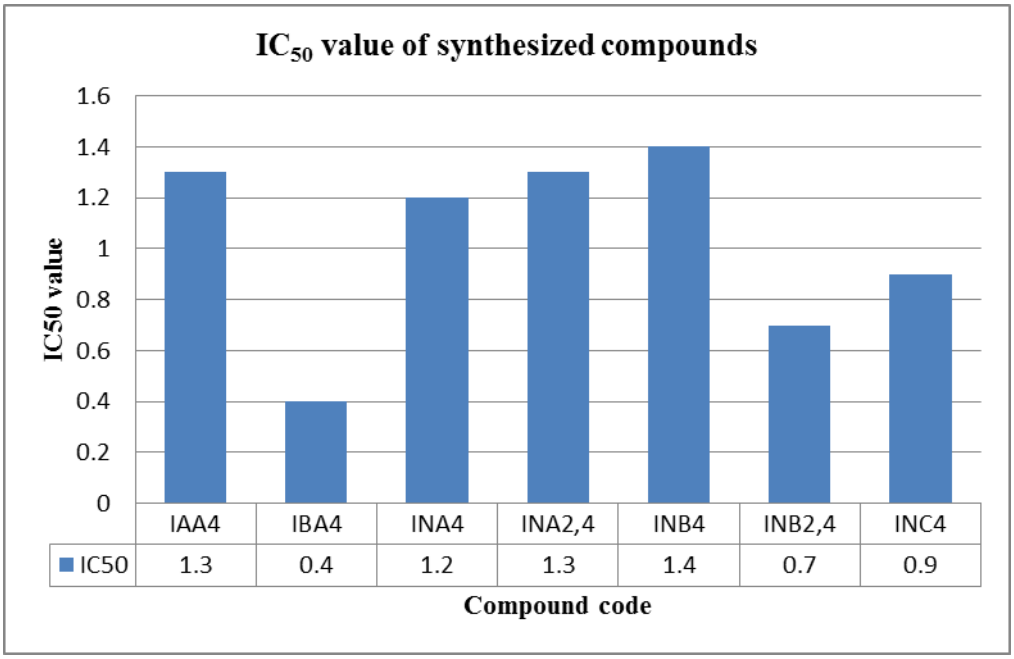


Figure 3: IC50 value of synthesized compounds.

I. REFERENCE

1. S. kavitha Bagya, P.V.Rajashree and Kishore Gnana Sam, Research journal of medicinal plant, 2011; 5: 728-737.
2. Mohammed Mahbubul Hoque and Mohammed Rabiul Islam, A journal of the Bangladesh Pharmacological Society, 2008; 3: 21-26.
3. Abolfazl olyaei, Bahareh shams, Mahdieh sadeghpour, Tetrahedron Letters, 2010; 51: 6086-6089.
4. Ali Irfan Ilbas, Umut Gonen, Semih Yilmaz, Mehmet Yasar Dadandi, Turkish Journal of Botany, 2012; 36: 263-268.
5. J.M. Khurana, Chemistry of Heterocyclic Compounds, 2006; 21-22.
6. Mohammed A. A., Radwan.A., Eman A. Ragab, Bioorganic & Medicinal Chemistry, 2007; 15: 3832–3841.
7. Mohammed Arifuzzaman, Rafiya Khan Kandahary and Md. Rabiul Islam, A Journal of the Bangladesh Pharmacological Society, 2009; 4: 96-100.
8. Mohammed Mahbubul Hoque and Mohammed Rabiul Islam, A journal of the Bangladesh Pharmacological Society, 2008; 3: 21-26.
9. O.P. Agarwal, Organic chemistry reactions and reagents, 2010; 47: 651-661.
10. OECD Guideline for testing of chemicals, 2004; 202: 1-5.