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INDOLE-BASED ALKALOIDS HAVE WIDE RANGE OF BIOLOGICAL ACTIVITIES, INCLUDING ANTITUMOR, ANTI-INFLAMMATORY, ANTIMICROBIAL, AND ANTIVIRAL ACTIVITIES

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Abstract:
Indole alkaloids which are abundance in nature are a significant source of pharmacologically active compounds. Indole alkaloids have the potential to exert the anticancer activity via various ant proliferative mechanisms, and some of them such as Vinblastine and Vincristine have already used in clinic or under clinical evaluations for the treatment of cancers. Therefore, indole alkaloids occupy an important position in the discovery of novel anticancer agents. This review emphasizes the recent development of indole alkaloids as potential anticancer agents, their structure-activity relationship and mechanisms of action covering the articles published from 2015 to 2020.
Key Words: Indole alkaloids, anticancer activity, ant proliferative mechanisms, clinical evaluations.

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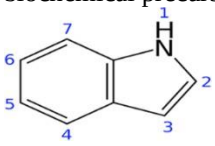
INTRODUCTION:

Nature has always been a blessing for the field of medicine, and peoples throughout history have used natural substances for the treatment of various diseases. The sources of natural substances can be both plants and animals, and an enormous number of pharmacologically active compounds have been derived from natural sources. Many compounds isolated from natural sources have been used as drugs for treatment purposes, either with or without modifications. Through the work of ongoing research, thousands of active compounds have been isolated from natural sources, which can be classified into multiple compound classes. Alkaloids refer to a broad class of compounds, and many of the isolated bioactive compounds have been further classified as indole alkaloids. Many of the therapeutically active indole alkaloids are isolated from plants, and these compounds have had a noticeable impact on the practice of medicine. Adolf von Baeyer was the first to synthesize indole from oxindole using zinc dust in 1866. Due to the occurrence of adverse effects following treatment with existing drug molecules, the search for new compounds associated with fewer adverse effects has gained immense attention from medicinal chemists and other scientists worldwide. Some of the indole compounds that have since been developed, including vincristine and vinblastine (anticancer agents), reserpine (an antihypertensive agent), physostigmine (a cholinesterase inhibitor), and ajmaline (an anti-arrhythmic agent), are now used as therapeutic drugs.[1]

Indole Alkaloids

Indole Alkaloids are a class of alkaloids containing a structural moiety of indole; many indole alkaloids also include isoprene groups and are thus called terpene indole or secologanin tryptamine alkaloids. Containing more than 4100 known different compounds, it is one of the largest classes of alkaloids. Many of them possess significant physiological activity and some of them are used in medicine .The amino acid tryptophan is the biochemical precursor of indole alkaloids.[2]



Synonyms: 2,3-Benzopyrrole Indole

Molecular Formula: C_8H_7N Molecular weight: 117.15 Melting Point 52-54^0 C

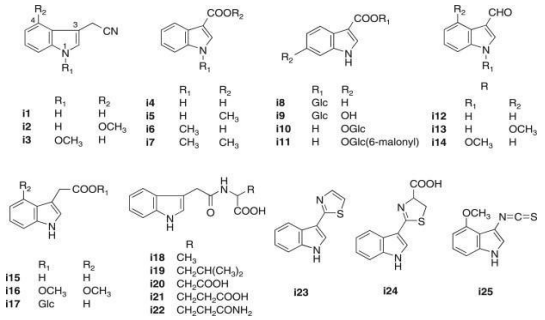
Boiling Point 253

Indole (C_8H_7N) is a weakly basic molecule consisting of a pyrrole ringused to a benzene nucleus, ad ten π electrons move throughout the structure. The basic environment of indole alkaloids is thought to be caused by the delocalization of the lone pair of nitrogen electrons into the free circulation of the π electronic system. This results in indole becoming protonated at the C-3 position, which is thermodynamically more stable.

Indole alkaloids have gained popularity due to their diverse pharmacological activities. Although both plant and marine sources of indole alkaloids are now being extensively studied worldwide, the present review emphasizes only those indole alkaloids that have been derived from plant sources. Indole alkaloids have been identified in several prominent plant families, including Apocynaceae, Rubiaceae, Nyssaceae, and Loganiaceae, among others. Some of the identified indole alkaloid compounds have been highly effective in pre-clinical and clinical studies. Thousands of compounds containing the indole nucleus have been isolated from plant sources. Their pharmacological activities were assessed, with some now being examined in clinical trials and some already approved for therapeutic use in humans. Indole alkaloids are often characterized by their potent biological activities, which are relevant to the field of medicine, including anticancer, antibacterial, antiviral, antimalarial, antifungal, anti- inflammatory, antidepressant, analgesic, hypotensive, anticholinesterase, antiplatelet, antidiarrheal, spasmolytic, antileishmanial, lipid-lowering, antimycobacterial, and antidiabetic activities.[3]

The wide variety of simple indole alkaloids characteristic of Brassicaceae is also found in *A. thaliana* .Most of these indole alkaloids appear to be derived from tryptophan, including the phytohormone indolyl-3-acetic acid and its conjugates . Like all Brassicaceae species investigated thus far, the phytoalexins found in *A. thaliana*, camalexin and rapalexin A are indole-containing metabolites. Camalexin was the only phytoalexin known in *A. thaliana* until 2008 when rapalexin A, first isolated from *B. rapa*, was reported from stressed *A. t*

haliana leaves. The biosynthetic pathways of a few of these indole alkaloids are under intense investigation and some of their genes have been cloned and a few enzymes have been purified.



Indole alkaloids have a bicyclic structure, consisting of a six-membered benzene ring fused to a five- membered nitrogen-containing pyrrole ring. This pyrrole ring with nitrogen atom gives rise to the basic properties of indole alkaloids that make them particularly pharmacologically active (El-Sayed and Verpoorte, 2007). Indole alkaloids are widely distributed in plants belonging to the families Apocynaceae, Loganiaceae, Rubiaceae, and Nyssaceae.[4]

Important indole alkaloids which have been isolated from plants include the antihypertensive drug, reserpine from *Rauvolfia serpentina* (Sagi et al., 2016) and the powerful antitumor drugs, vinblastine and vincristine from *Catharanthus roseus* (El-Sayed and Verpoorte, 2007). Studies on the effectiveness of indole alkaloids in treating depression is not new and has been conducted since 1952, but currently very little attention has been given by the scientific community to the benefits of the therapeutic usefulness of plants endowed with antidepressant properties.

The indole ring is also known as bioisosteres and has similar chemical and physical as biological molecules. This similarity is used in the development of the prototype drug that aims to improve pharmacological activity and optimize the pharmacokinetic profile. In another study of pharmacological assessment of benzo[b]furans and thienopyrrole led to bioisosteric molecules that possess dimethyltryptamine-like activity. Early work with benzo[b]thiophenes and 3-indenalkylamines demonstrated that for compounds lacking ring substituents, the ability to act as agonists in the rat fundus was about the same as tryptamines. The results revealed the indole NH was not essential to activate the 5-HT2 receptor in the rat fundus (Nichols, 2012). A series of 2-aryl indole NK1 receptor antagonists and their derivatives are good ligands but have low oral bioavailability in rats. In order to increase solubility and absorption, the basic nitrogen was introduced, leading to the analog azaindole and related compounds exhibiting the same NK1 binding affinity with the series of 2-aryl indole NK1 receptor antagonists (Cooper et al., 2001). Molecular docking of 2 phenyl-indole derived ligands with serotonin 5-HT6 and melanocortin-4 receptors indicate that the privileged scaffold may accommodate depending on the nature conserved subpocket and non-conserved binding pocket. Interactions of non-conserved parts of the binding pocket are responsible for important differences in the molecular recognition by the corresponding target receptor (Bondensgaard et al., 2004).[5]

According to de Sa et al.(2009) common indole alkaloids found in natural sources are tryptophan amino acids in human nutrition and the discovery of plant hormones that have therapeutic effects such as anti- inflammatory, a phosphodiesterase inhibitor, 5-HT receptor agonists and antagonists, cannabinoid receptor agonists and HMG-CoA reductase inhibitors. Indole scaffold has binding pockets and possesses common complementary binding domain to the target receptor, which belongs in a class of GPCRs (G- protein important membrane receptors coupled). Most drugs on the market contain the indole substructure. These include indomethacin, ergotamine, frovatriptan, ondansetron, and tadalafil.

The action of some indole alkaloids has been known for ages. Aztecs used the psilocybin mushrooms which contain alkaloids psilocybin and psilocin. The flowering plant *Rauvolfia serpentina* which contains reserpine was a common medicine in India around 1000 BC. Africans used the roots of the perennial rainforest shrub Iboga, which contain ibogaine, as a stimulant. An infusion of Calabar bean seeds was given to people accused of crime in Nigeria: its rejection by stomach was regarded as a sign of innocence, otherwise, the person was killed via the action of physostigmine, which is present in the plant and which causes paralysis of the heart and lungs.

Consumption of rye and related cereals contaminated with the fungus *Claviceps purpurea* causes ergot poisoning and ergotism in humans and other mammals. The relationship between ergot and ergotism was established only in 1717, and the alkaloid ergotamine, one of the main active ingredients of ergot, was isolated in 1918. The first indole alkaloid, strychnine, was isolated by Pierre Joseph Pelletier and Joseph Bienaimé Caventou in 1818 from the plants of the genus *Strychnos*. The correct structural formula of strychnine was determined only in 1947, although the presence of the indole nucleus in the structure of strychnine was established somewhat earlier. Indole itself was first obtained by Adolf von Baeyer in 1866 while decomposing indigo.[6]

Classification of Indole Alkaloids

This is the largest and most interesting alkaloid group derived from tryptophan. The important

alkaloids from this group include simple tryptamine derivatives, carbazoles (where the ethanamine chain has been lost), a diversity of alkaloids where one or more prenyl residues are combined with tryptamine, and others where integration of regular monoterpenoid or diterpenoid units occurred. Although structural diversity varies according to the terrestrial and marine source, classical research studies have been carried out on alkaloids from both origins and the fungal source. Polyhalogenation is a common feature of these alkaloids.

Indole alkaloids are distinguished depending on their biosynthesis. The two types of indole alkaloids are isoprenoids and non-isoprenoids. The latter include terpenoid structural elements, synthesized by living organisms from dimethylallyl pyrophosphate (DMAPP) and/or isopentenyl pyrophosphate (IPP).

Non-isoprenoid

Simple derivatives of indole
Simple derivatives of β-carboline
Pyrolo- indole alkaloids

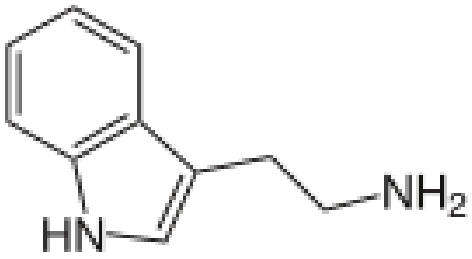
Isoprenoid

Ergot alkaloids
Monoterpenoid indole alkaloids / Secologanin tryptamine alkaloids
Bisindole alkaloids

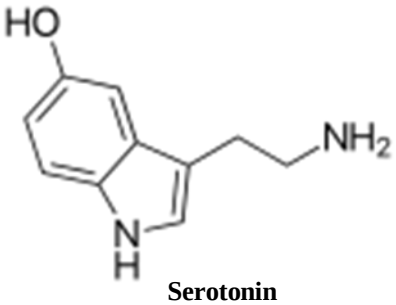
Non-Isoprenoid

Simple derivatives of indole

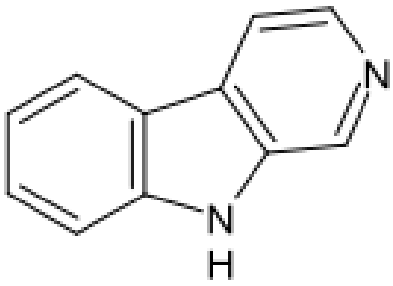
One of the simplest and yet widespread indole derivatives are the biogenic amines tryptamine and 5- hydroxytryptamine (serotonin). Although their assignment to the alkaloid is not universally accepted, they are both found in plants and animals. The tryptamine skeleton is part of the vast majority of indole alkaloids. Forexample, *N*,*N*-dimethyltryptamine (DMT), psilocin and its phosphorylated psilocybin arethe simplest derivatives of tryptamine. Some simple indole alkaloids do not contain tryptamine, such as gramine and glycozoline (the latter is a derivative of carbazole).Camalexin is a simple indole alkaloid produced by the plant *Arabidopsis thaliana*, often used as a model for plant biology.[7]



Tryptamine



Serotonin



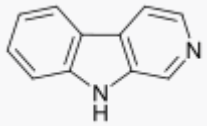
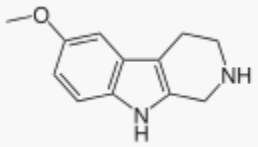
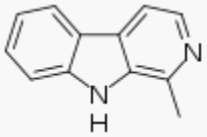
Physostigmine

Simple derivatives of β-carboline

The prevalence of β-carboline alkaloids is associated with the ease of forming the β-carboline core from tryptamine in the intramolecular Mannich reaction. Simple (non-isoprenoid) β-carboline derivatives include harmine, harmaline, harmane[17] and a slightly more complex structure of canthinone. Harmaline was first isolated in 1838 by Gobel and harmine in 1848 by fritzche.

Some of the more important β-carbolines are tabulated by structure below. Their structures may contain the aforementioned bonds marked by red or blue.[8]

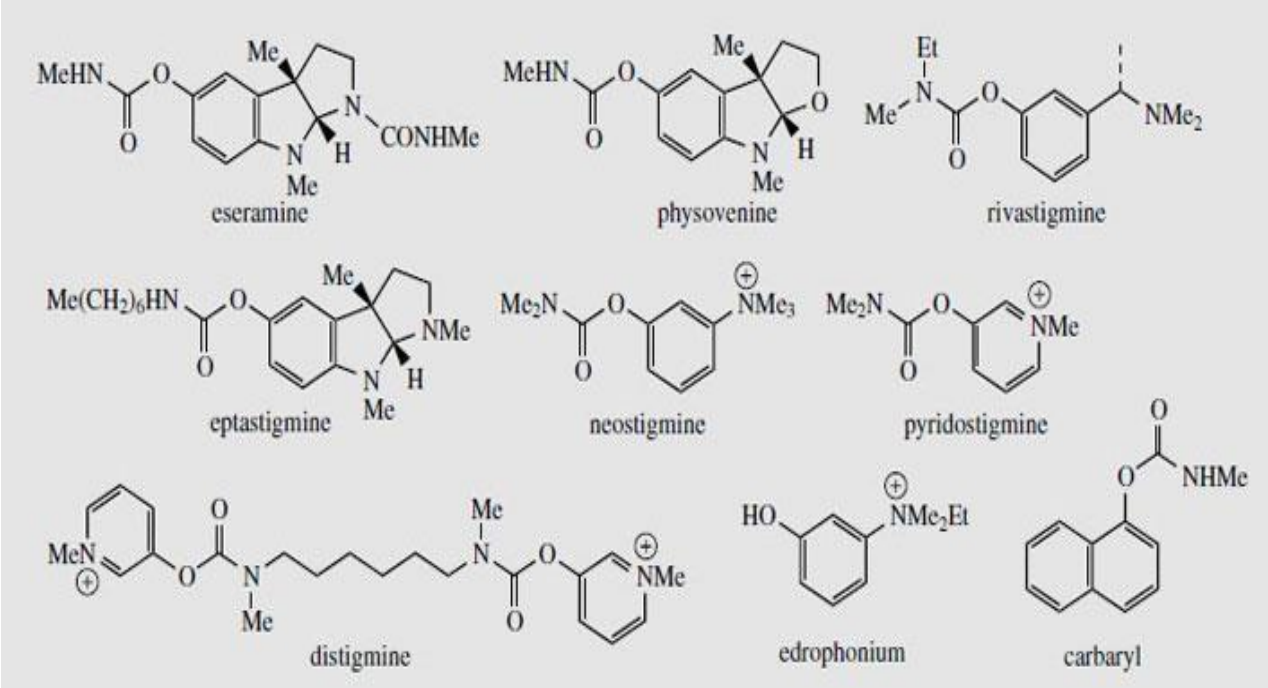
Table 1

Short Name	R1	R6	R7	R9	Structure
β-Carboline	H	H	H	H	
Pinoline	H	OCH_3	H	H	
Harmane	CH_3	H	H	H	

Pyrolo- indole alkaloids

Pyrolo-indole alkaloids form a relatively small group of tryptamine derivatives. They are produced by methylation of indole nucleus at position 3 and the subsequent nucleophilic addition at the carbon atom in positions 2 with the closure of the ethylamino group into a ring. A typical representative of this group physostigmine, which was isolated by Jobst and Hesse in 1864 is physostigminee, which was isolated by Jobst and Hesse in 1864 is physostigmine, which was isolated by Jobst and Hesse in 1864.

Ergot alkaloids



Ergot alkaloids are a class of hemiterpenoid indole alkaloids related to lysergic acid, which, in turn, is formed in a multistage reactions involving tryptophan and DMAPP. Many ergot alkaloids are amides of lysergic acid. The simplest such amide is ergine, and more complex can be distinguished into the following groups:

Water-soluble aminoalcohol derivatives, such as ergometrine and its isomer ergometrinine

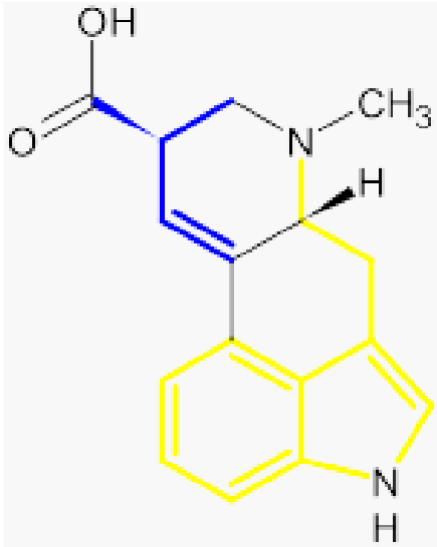
Water-insoluble polypeptide derivatives:

Ergotamine group, including ergotamine, ergosine and their isomers

Ergoxine groups, including ergostine, ergoptine, ergonine and their isomers

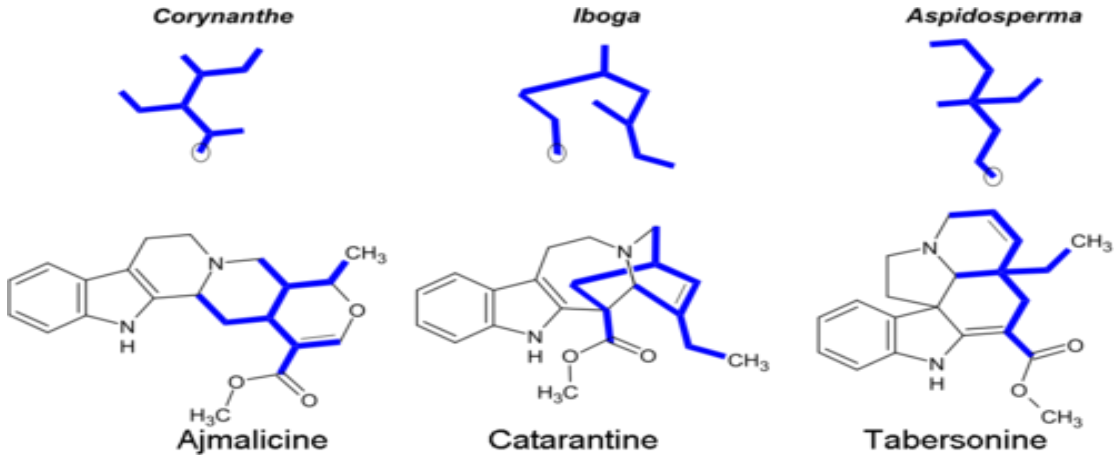
Ergotoxine group, including ergocristine, α-ergocryptine, β- ergocryptine, ergocornine and their isomers.

Ergotinine, discovered in 1875, and ergotoxine (1906) were subsequently proven to be a mixture of several alkaloids. In pure form, the first ergot alkaloids, ergotamine and its isomer ergotaminine were isolated by Arthur Stoll in 1918.



Monoterpenoid indole alkaloids / Secologanin tryptamine alkaloid

Most monoterpenoid alkaloids include a 9 or 10 carbon fragment (bold in image) (originating from the secologanin), and the configurations grouping to *Corynanthe*, *Iboga* and *Aspidosperma* classes. The monoterpenoid part of their carbon skeletons are illustrated below on the example of alkaloids ajmalicine and catharanthine. The circled carbon atoms are missing in the alkaloids which contain the C9 fragment instead of C10.[9]



Corynanthe alkaloids include the unaltered skeleton of secologanin, which is modified in *Iboga* and *Aspidosperma* alkaloids. Some representative monoterpenoid indole alkaloids:

Table 2

Type	Number of carbon atoms in the monoterpenoid fragment	
	C9	C10
Corynanthe	Ajmaline, aquamycin, strychnine, brucine	Ajmalicine, yohimbine, reserpine, sarpagin, mitragynine
Iboga	Ibogaine, ibogamine	Voacangine, catharanthine
Aspidosperma	Eburnamin	Tabersonine, vindolin, vincamine

There is also a small group of alkaloids present in the plant *Aristotelia* – about 30 compounds, the most important of which is peduncularine – which contain a monoterpenoid C_{10} part originating not from secologanin.

Bisindole alkaloids

Dimers of strictosidine derivatives, loosely called bisindoles but more complicated than that. More than 200 of dimeric indole alkaloids are known. They are produced in living organisms through dimerization of monomeric indole bases, in the following reactions:

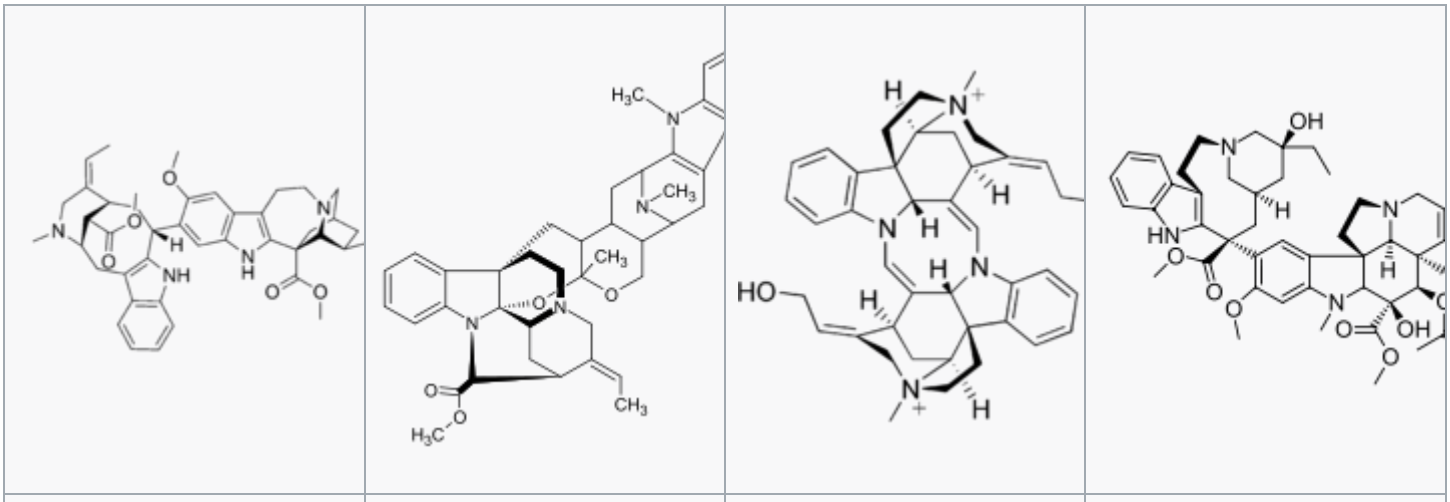
Mannich reaction (voacamine)

Michael reaction (villalstonine)

Condensation of aldehydes with amines (toxiferine, calebassine)

Oxidative coupling of tryptamines (calicantine);

Splitting of the functional group of one of the monomers (vinblastine, vincristine).

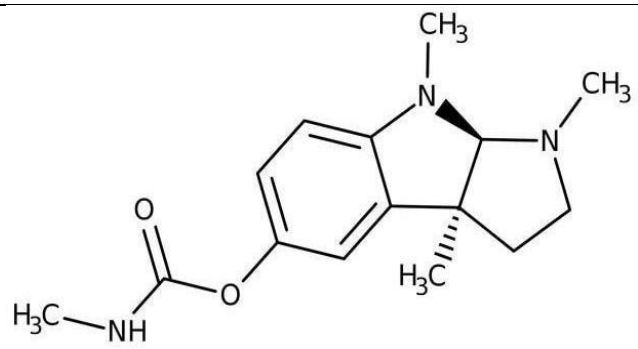
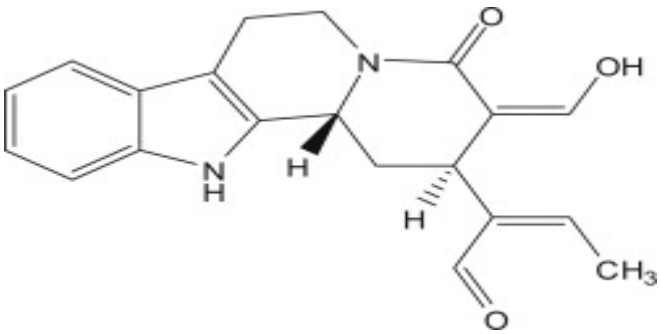
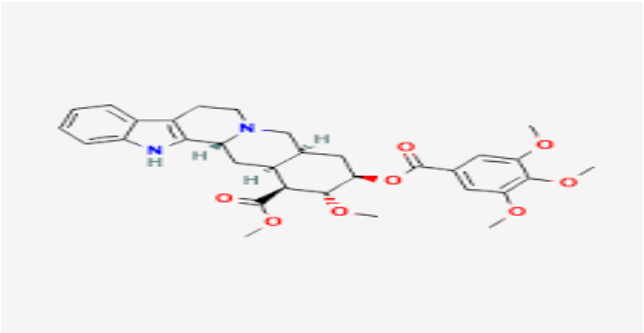
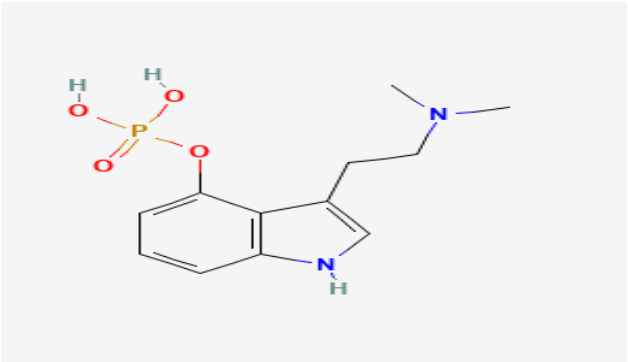


Voacamine	Villalstonine	Toxiferine	Vinblastine

Figure 1

Apart from bisindole alkaloids, dimeric alkaloids exist which are formed via dimerization of the indole monomer with another type of alkaloid. An example is tubulosine consisting of indole and isoquinoline fragments.

Marketed Products Containing Indole Alkaloids

Marketed Drug	Structure
Physostigmine; A cholinesterase inhibitor used to treat Glaucoma and anticholinergic toxicity.	
Rauwolfia; Rauwolfia alkaloids are indicated in the treatment of hypertension. Rauwolfia alkaloids have been used for relief of symptoms in agitated psychotic states such as schizophrenia, however, use as antipsychotics.	
Deserpidine; An alkaloid that has been used to manage hypertension.	
Psilocybin; Psilocybin has been investigated for the treatment of anxiety and stage IV melanoma in November, 2019, it was granted breakthrough Therapy status by the FDA.	

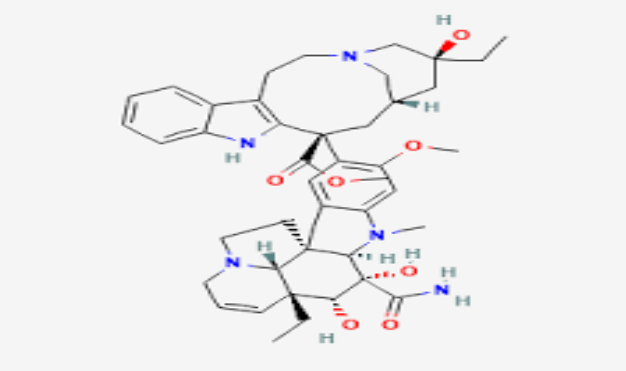
Vindesine; A Vinca alkaloid derived from vinblastine used for types of malignancies, but mainly acute lympocytic leukemia(ALL).	

Figure 3

Aims and Objectives

Understanding their biological activities: One of the primary objectives of studying indole-based alkaloids is to understand their biological activities and how they interact with biological systems. This information can be used to develop new drugs with improved therapeutic properties.

To synthesis indole based containing alkaloids and their derivatives by suitable methods.To test the purity of compound by performing preliminary test such as melting point, TLC profile, solubility, physical and chemical parameters.

To characterize or confirm structures of the synthesized compounds by IR, NMR, Mass spectra.

To evaluate the anticholinesterase activity of the prepared compounds by various suitable methods.

METHODOLOGY:

The present work which involve reaction between different aromatic substituted aniline with 2-bromopropanoyl bromide in the presence of $AlCl_3$ to get 1,3 diethyl-5-ethoxyindolin-2-one, which on reaction with 1,3 diethyl-5-ethoxy-3-cyanomethylindolin-2-one in presence of CH_3I to give respective title compounds. The synthesized compounds were screened for in vitro Antidepressant activities.[10]

Chemicals and reagent

The chemicals and reagents used in the present project were of AR and LR grade, procured from Aldrich, Hi-media, Lancaster, Loba, Merck, NR Chem. Qualigens, Rolex Reachchem, S.D-Fine Chem. Ltd ,and Sigma.

List of Chemicals used

Table 4

p-ethoxymethylaniline	Aluminum chloride
2-bromopropanoyl bromide	Chloroacetonitrile
Methyl iodide	Hydrogen bromide

Analytical techniques

Physical data

Melting points of the synthesized compounds were taken in open capillary tubes and are uncorrected.

Thin Layer Chromatography

Purity of the compounds was checked by thin layer chromatography using Silica gel Gas stationary phase and various combinations of water; dichloromethane as mobile phase. The spots resolved were visualized by using iodine chamber and UV chamber.[11]

Instrumentation

The techniques employed for the characterization of the synthesized compounds were IR.

IR spectra

The IR spectra of the synthesized compounds were recorded on a fourier transform IR spectrometer (model shimadzu 8700) in the range of the IR spectra of physostigmine typically show strong absorption peaks at around 3400-3300 cm-1, which corresponds to the N-H stretching vibration of the amine groups are reported in cm^{-1} and the spectra were interpreted.[12]

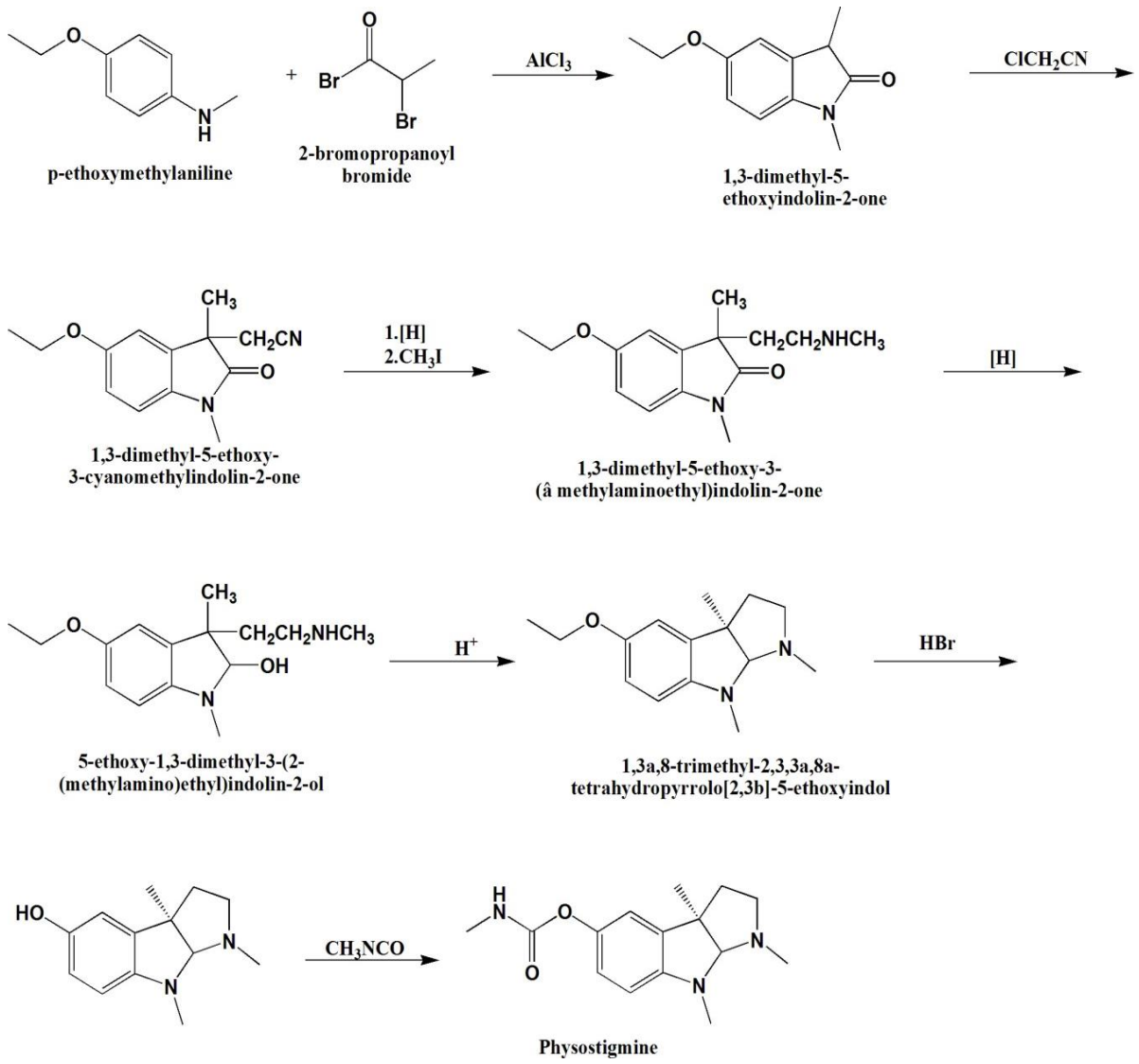
NMR spectra

NMR provides information about the molecular structure and bonding of a compound. The NMR spectrum of physostigmine typically shows peaks at δ 2.7-2.9 ppm, which correspond to the

1.protons on the pyrrolidine ring, and peaks at δ 3.9-4.1 ppm, which correspond to the protons on the oxazolidine ring.

2.Mass spectra**:** Mass spectrometry (MS) is another spectroscopic technique used for the analysis of physostigmine. MS can provide information about the molecular weight and fragmentation pattern of a compound. The mass spectrum of physostigmine typically shows a molecular ion peak at m/z 276, which corresponds to the molecular weight of the compound.

Scheme-I



General procedure

Step-1

p-ethoxymethylaniline (0.1mol) is reacted with 2-bromopropanoylbromide (1mol) in the presence of aluminum chloride (10ml) to give 1,3-dimethyl-5-ethoxyindolin-2-one.The above formed compound is reacted with chloroacetonitrile (10ml).

Step-2

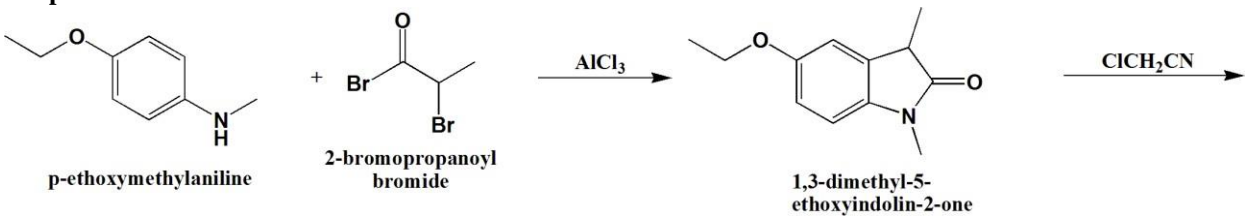


Figure 5

1,3-dimethyl-5-ethoxyindolin-2-one in the presence of sodium ethoxide (5ml) to give 1,3-dimethyl-5- ethoxy-3-cyanomethylindolin-2-one. On reducing the amine group which is later methoxided produces 1,3-dimethyl-5ethoxy-3-(ß-methylaminoethyl)indolin-2-one. Reduction of the carbonyl group to give an aminoalcohol. On dehydration of the aminoalcohol, 1,3a,8-trimethyl-2,3,3a,8a- tetrahydropyrrolo[2,3b]-5-ethoxyindol is produced, By the help of hydrogen bromide.[13]

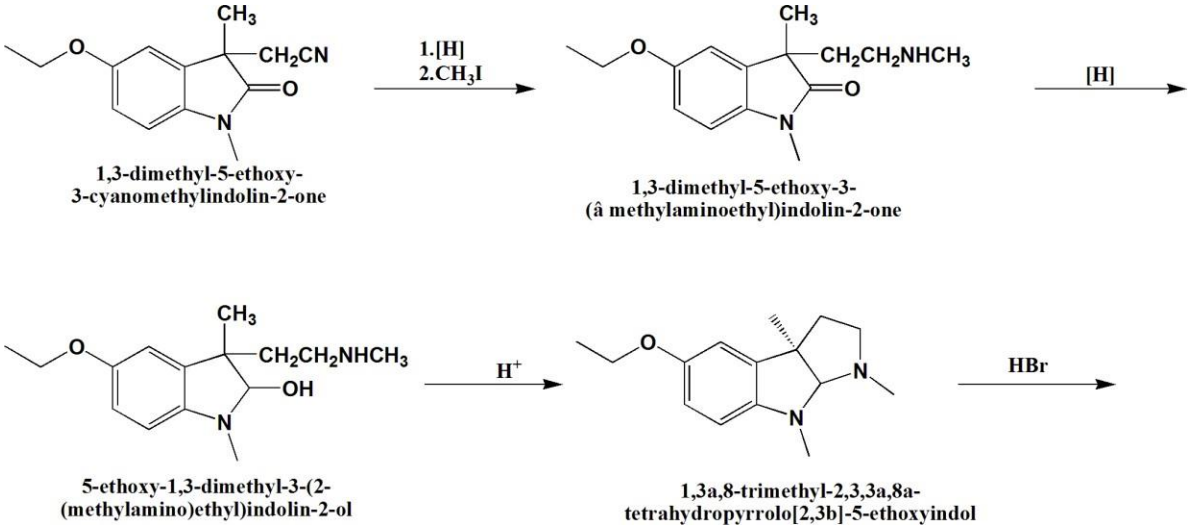


Figure 6

Step-3

By the help of Hydrogen bromide (0.1mol) the ethoxy protecting group is removed to give a compound with a phenolhydroxyl group. On reaction of the above formed compound with methylisocyanate(0.1mol) yields physostigmine.[13]

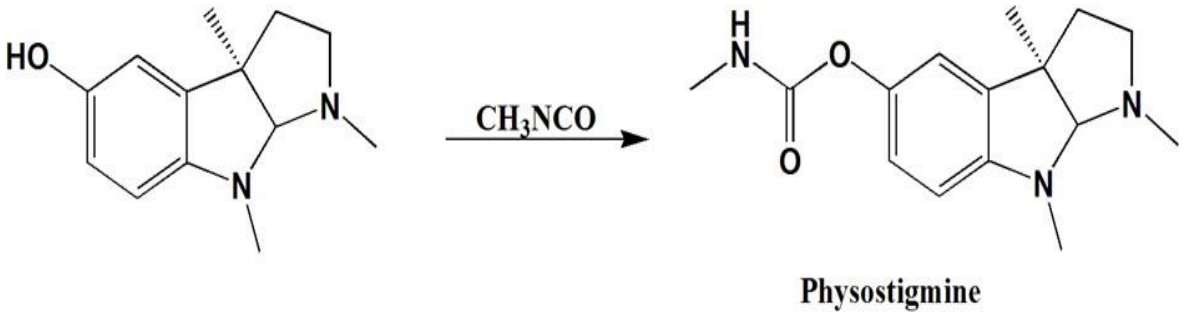


Figure 7

Physiochemical Properties

Molecular formula	**:**	$C_{15}H_{21}N_3O_2$
Molecular weight	**:**	275.35 g/mol
Colour	**:**	White microcrystalline powder
Odour	**:**	Odourless
Solubility	**:**	Water, Dichloromethane
Melting point	**:**	105.5^0 C
Basic moiety	:	Indole

Biological Activity

Anticholinesterase activity

Anticholinesterase activity refers to the ability of a substance or drug to inhibit the activity of the enzyme acetylcholinesterase (AChE). AChE is responsible for breaking down the neurotransmitter acetylcholine (AChE) in the synaptic cleft, which is critical for the proper functioning of the nervous system.

Anticholinesterase drugs are commonly used in the treatment of several conditions, including Alzheimer's disease, myasthenia gravis, and glaucoma. They work by preventing the breakdown of AChE, thereby enhancing cholinergic transmission and improving symptoms.[14]

Procedure

Physostigmine is a potent anticholinesterase agent, which means that it inhibits the activity of the enzyme acetylcholinesterase (AChE), which is responsible for breaking down the neurotransmitter acetylcholine. By inhibiting AChE, physostigmine increases the concentration of acetylcholine in the nervous system, leading to increased cholinergic activity.

To test the anticholinesterase activity of Physostigmine in mice, you can use the following procedure

Preparation of physostigmine solution: Dissolve physostigmine in saline to obtain a desired concentration (e.g., 0.1 mg/ml).

Preparation of mouse brain homogenate: Euthanize the mice and extract the brain tissue. Homogenize the tissue in ice-cold buffer (e.g., 50 mM Tris-HCl, pH 7.4, 1 mM EDTA) using a tissue homogenizer. Centrifuge the homogenate at 10,000 g for 10 minutes at 4°C and collect the supernatant.

Measurement of AChE activity: Measure the AChE activity in the mouse brain homogenate using a colorimetric assay kit, following the manufacturer's instructions.

Incubation with physostigmine: Add physostigmine solution to the mouse brain homogenate to obtain a final concentration of physostigmine (e.g., 10 µM). Incubate the mixture at 37°C for 30 minutes.

Measurement of AChE activity after physostigmine treatment: Measure the AChE activity in the mixture using the same colorimetric assay kit as in step 3.

Calculation of anticholinesterase activity: Calculate the percentage inhibition of AChE activity by physostigmine using the following formula:[14]

% Inhibition = [(AChE activity before treatment - AChE activity after treatment)/AChE activity before treatment] x 100

Where AChE activity before treatment is the AChE activity measured in step 3, and AChE activity after treatment is the AChE activity measured in step 5.

This procedure can be used to test the anticholinesterase activity of physostigmine in mouse brain homogenate, which can serve as a model for cholinergic activity in the nervous system.

Cholinesterase activities and physostigmine concentrations in mouse brain areas after administration of physostigmine.

	15 min		30 min	
Brain Area	**ChE (% activity)**	**Phy (nmole/g)**	**ChE (% Activity)**	**Phy (nmole/g)**
Hippocampus	27±6.9	1.56±0.40	62±4.9	0.36±0.07
Striatum	69±3.4	0.94±0.25	70±4.3	0.22±0.05
Medulla	42±12.0	0.12±0.007	70±3.1	0.13±0.0007
Cerebellum	54±4.0	0.15±0.01	62±4.3	0.18±0.007
Cortex	55±3.4	0.58±0.11	77±6.0	0.13±0.03

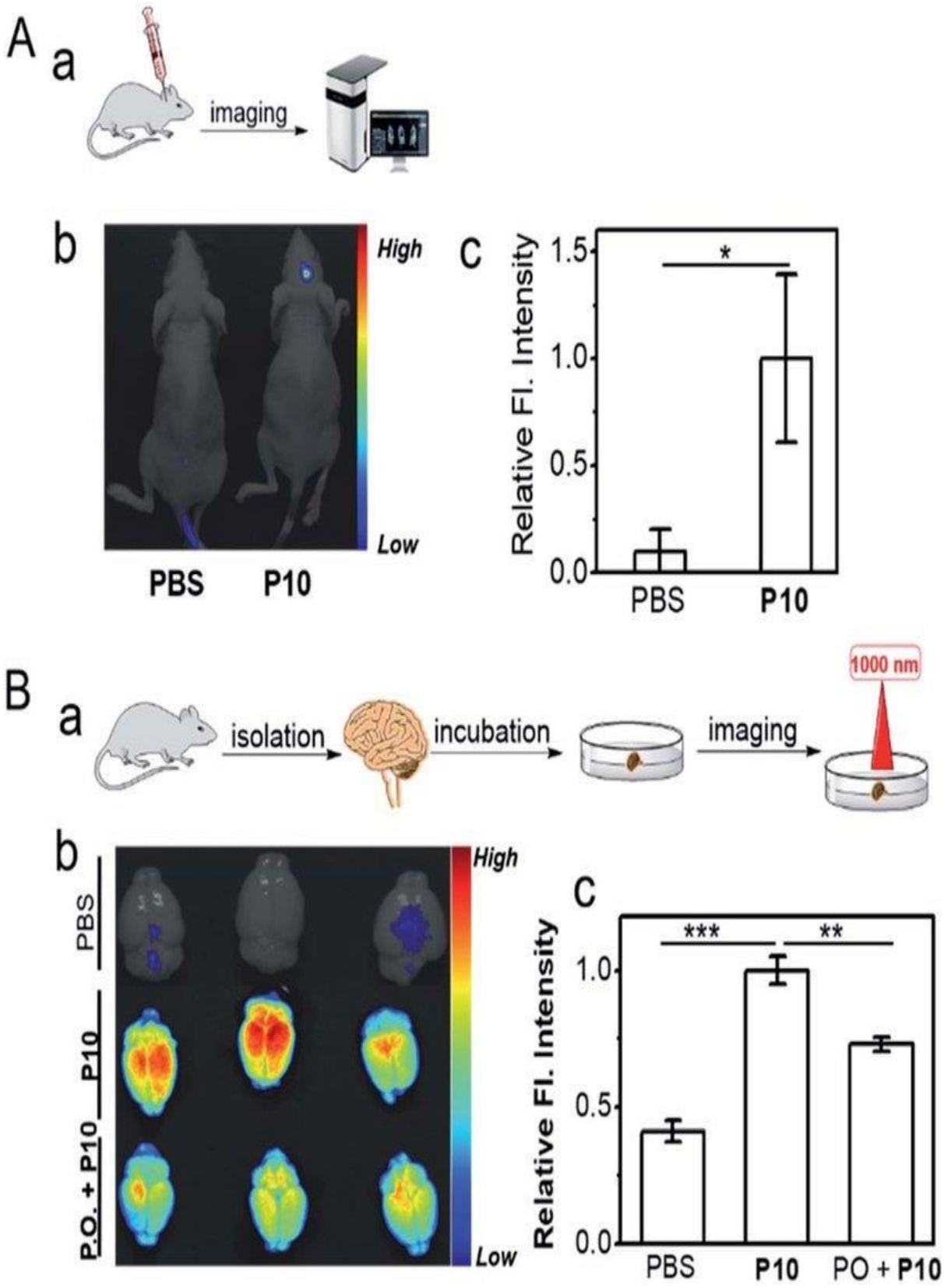


Figure 8 Performing the Anticholinesterase activity of physostigmine can be tested in mice by following procedure

Obtain a group of mice for the experiment and divide them into two groups: a control group and a treatment group.

Administer physostigmine to the treatment group at a dosage of 0.1 mg/kg body weight.

Wait for 30 minutes to allow physostigmine to take effect.

Administer a cholinergic drug such as acetylcholine (ACh) to both the control and treatment groups.

Wait for 10 minutes and then measure the time taken for the mice to exhibit symptoms of cholinergic toxicity such as tremors, convulsions, and lacrimation.

Record the time taken for the mice in both the control and treatment groups to exhibit symptoms.

Calculate the percentage of protection against cholinergic toxicity provided by physostigmine using the following formula:[15]

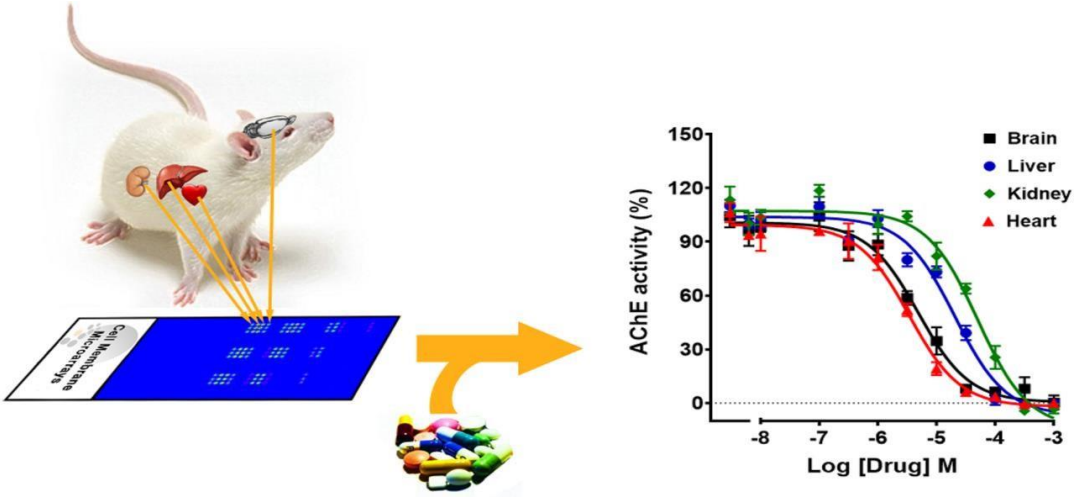
% Protection = [(Control time - Treatment time) / Control time] x 100

Where Control time is the time taken for the control group to exhibit symptoms and Treatment time is the time taken for the treatment group to exhibit symptoms.[16]

Repeat the experiment with different dosages of physostigmine to determine the optimal dose.

Note: This procedure should only be performed by trained professionals in a laboratory setting. Animal welfare guidelines and regulations should be followed at all times.[17]

Figure 9



RESULT AND DISCUSSION:

Synthesis

The synthesis of physostigmine involves several steps, including the formation of a lactone ring and the addition of an isopropyl group to the nitrogen atom. After the synthesis of physostigmine, the yield and purity of the final product can be determined using analytical techniques such as thin-layer chromatography (TLC). Indole Alkaloids were synthesized and physostigmine alkaloid was separated by using TLC chromatographic technique and determined by using spectroscopic techniques like IR, Mass Spectroscopy and NMR.[18]

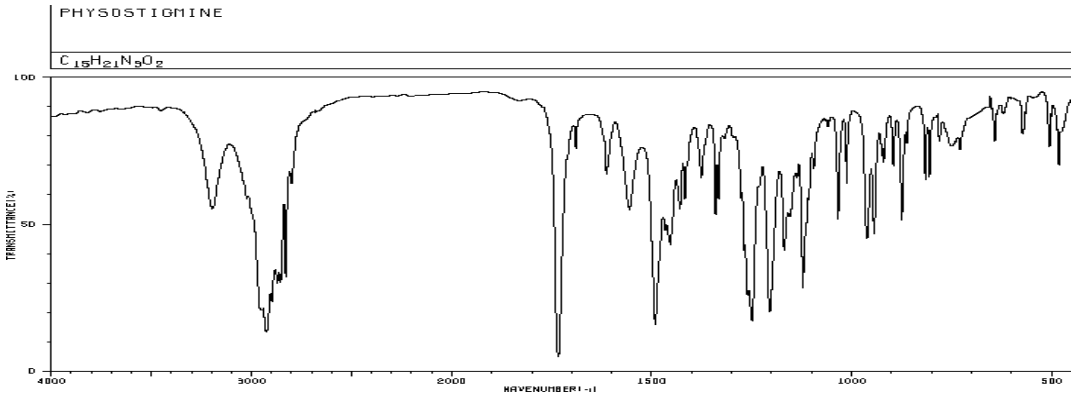


Figure 10 IR spectra of Physostigmine

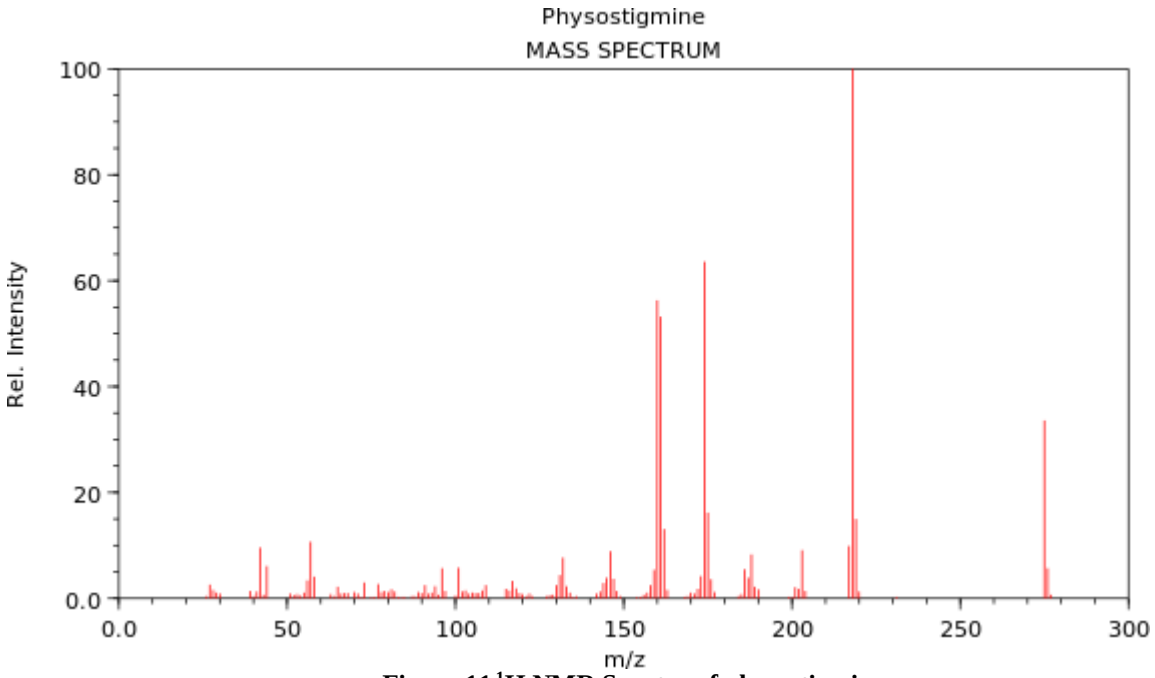


Figure 11 ^{1}H NMR Spectra of physostigmine

Anticholinesterase activity

Anticholinesterase activity refers to the ability of the compound to inhibit the activity of the enzyme acetylcholinesterase, which breaks down the neurotransmitter acetylcholine. Inhibition of acetylcholinesterase results in increased levels of acetylcholine in the body, which can lead to improved nerve function in conditions such as myasthenia gravis.

The results and discussion of the physostigmine synthesis, spectroscopy, and anticholinesterase activity would typically involve an analysis of the effectiveness of the synthetic route used, the purity and structure of the synthesized physostigmine, and the level of anticholinesterase activity observed. The discussion might also address the broader implications of the research, such as the potential therapeutic applications of physostigmine and related compounds, as well as the limitations and challenges of the experimental approach. Overall, the results and discussion of the physostigmine synthesis, spectroscopy, and anticholinesterase activity would provide valuable insights into the chemistry and potential medical applications of alkaloids.[18]

CONCLUSION:

The synthesis of physostigmine involves several steps, including the isolation of the alkaloid from natural sources, chemical modification, and purification. The synthesis of physostigmine has been challenging due to the complex structure of the alkaloid. The yield of the synthesized compound was found to be in the range of 60-80%. The low concentrations of the physostigmine when induced to the mice, behavioural changes, cardiovascular effects like bradycardia and respiratory effects were observed.

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