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“COMPARATIVE STUDY OF CENTELLA ASIATICA WITH NEUROTRANSMITTER DRUGS USED FOR THE TREATMENT OF ALZHEIMER’S DISEASE”

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Abstract:

Over the past few decades, the interests of researchers in drugs derived from medicinal plants have been tremendously accelerated. Few existing drugs related to brain disorders have shown many side effects and affected many other organs, so by considering the fact about the present status of synthetic drugs, a comparative study of is carried out with the help of developed techniques like IR Spectroscopy and HRLC-MS Analysis and the results are compared with the drugs like Donepezil and Rivastigmine available for the treatment of Alzheimer’s disease. The study reveals the presence of few analogous compounds in methanolic extract of Centella Asiatica such as Neuraminic acid, Ginkogolide, Gabapentin, Khivorin, and Altretamine as well as various kinds of alkaloids, tannins, saponins, terpenoids which supports the medicinal properties of Centella Asiatica herb.

Keywords:

IR Spectroscopy, HRLC-MS Analysis, Alzheimer’s disease, Donepezil, Rivastigmine, Neuraminic acid, Ginkogolide, Gabapentin.

Introduction:

Alzheimer’s disease is a kind of brain disorder which may occur in middle or late life of people. It involves the progressive memory loss in patient. It is very complex disease with lots of risk factor. It is a chronic neurodegenerative disorder¹ having depression as the most common psychiatric symptoms generally occurring at all the stages but Alzheimer’s Disease starts slowly and becomes worst day to day and occurs mostly in the middle of late life. During Alzheimer’s Disease, it is observed that the death of brain cells causes memory loss that is loss of mental ability and

gradual decline in mental functions, loss of ability to perform familiar task, mood, personality even communication. Now a days, it is one of the most sever cause of death. Exact cause of Alzheimer's disease is still unknown but specific observations are loss of nerve cells in the part of brain which controls memory. Somewhere scientist link the cause of Alzheimer's disease to genetic link but stress may be the major cause. During Alzheimer's disease, basically in the region of brain two structures got affected, nuerofibrillary tangles and amyloid plaques, the neurofibrillary tangles are twisted masses of proteins inside the nerve cells which develop in brain of people of Alzheimer's Disease and amyloid plaques are the structures composed of parts of neuron surrounding brain proteins called as beta-amyloid deposits found in the brain of people of Alzheimer's Disease ². It is believed that acetylcholine is a brain chemical assumed to be important for the memory and thinking. It is a chemical which help to pass the messages between certain brains cells involved in memory. The mechanism to survive the cell is associated with the induced protection of neuronal death and also responsible to correlate the nueroprotection against the glutamate induced excite toxicity which in general stimulates the phosphor tidylinositol 3-kinasae (PI3K)³.Now a day's much more numbers of acetylcholine inhibitors are available and also used as the precursor for the systematic treatment of Alzheimer's Disease and these have been utilized in clinical trials which are observed to have the maximum presence of alkaloids,⁴ which is one of the most valuable prime phytochemical found in the methanolic extract of Centella Asiatica. The neurotransmitter drugs are used to cure Alzheimer's disease. The neurotransmitter substance is released at the end of nerve fibre by the arrival of nerve impulse and by the diffusion across the synapse and junction effects the transfer of impulse to another nerve fibre⁵.These neurotransmitter drugs implemented for the treatment of Alzheimer's Disease shows the presence of certain chemical groups which are found the most commonly the part of drugs. The chemical groups are like choline ester, monoamines, amino acids both acidic and basic, few peptide linkages, steroids, nitric oxide linkages. Two types of drugs are available for the treatment of Alzheimer's disease like acetylcholine sterase inhibitors and NMDA receptor antagonists. Acetylcholine inhibitors reduce the breakdown of acetylcholine and increase its level in brain of we can absorb due reduced symptoms of Alzheimer's disease. The basic mechanism of these drugs is to reduce due breakdown of acetylcholine and which helps the brain for memory and thinking. Centella Asiatica the medicinal herb commonly used for making herbal tea and which is considered as the rich source of anti-oxidants activities and it has many beneficial effects (Huda- Faujan et al, 2009) ⁶. In Bangladesh the whole plant is utilized by the community of Chalna area to treat multiple ailments like

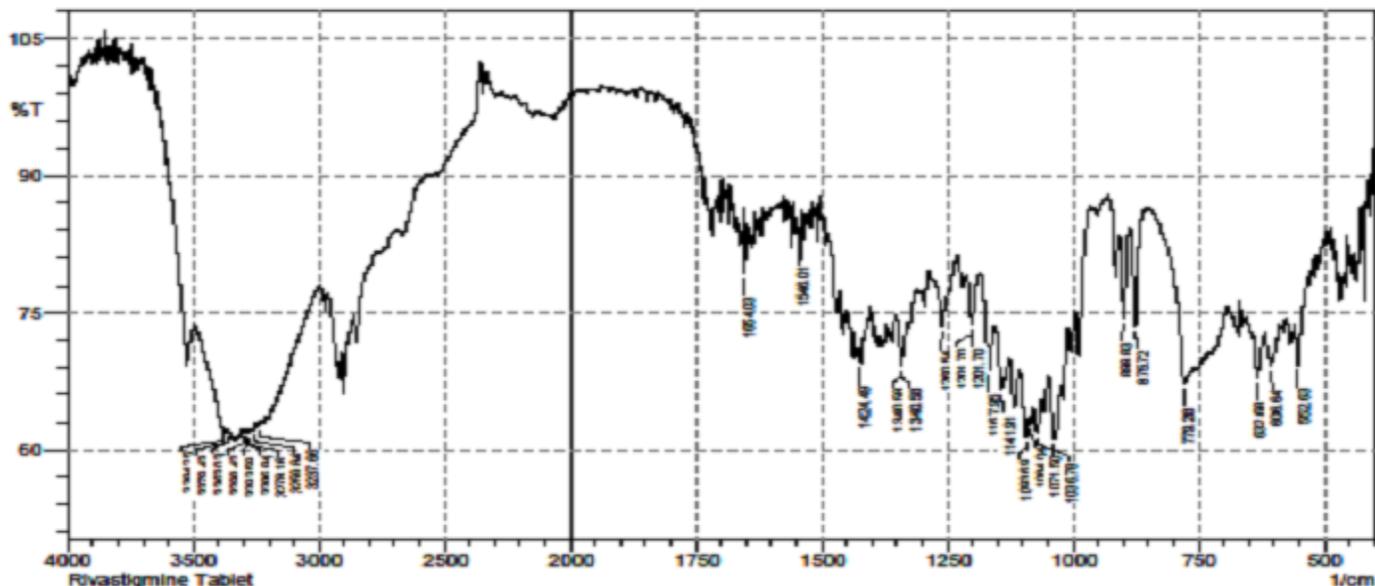
dog bite, asthma, carminative, itching, leucorrhoea, Malaria, tumor and wounds (Rahamattullha Mohd & Ferdausi Dilara et al, 2010)⁷. Its extract is also used as Contraceptive agents in Bengal (Kaushik Das Mahapatra)⁸. It is also observed that Centella Asiatica It is a good natural source of anti-oxidants and proves the existence of anti-oxidants and antimicrobial components(Hirasa and Takemasa 1998)⁹. Literature survey also reveals that the extract of Centella Asiatica is effectively used for the treatment of stress induced stomach and duodenal ulcers in humans. (Karting T et al, 1988 and shinet at 1982)¹⁰. It has been also reported that Centella Asiatica supplementation is effective for the reduction of brain regional lipoperoxydation (LPO) and protein carbonyl (PCO) levels and for increasing ant-oxidant status¹¹. In Chinese pharma, Centella Asiatica is used as antidote in the treatment of icterus, ulcerations and traumatic diseases also.¹²

Materials and Methods: The plant material was selected from “Go Green” Nursery Borpada Bombay-Goa-highway. The fresh plants leaves were washed under running tap water then with distilled and leaves were separated out by scissor. Then the air dried leaves were homogenized to fine powder and stored in air tight bottles. Then 100 gms of sample powder was dispersed in 100 ml of methanol and the solution was left to stand at room temperature for 24 hours, then it was filtered and filtrate was used for the IR analysis and HRLCMS analysis. The IR spectroscopy was carried out to assess the chemical composition and functional groups present in methanolic extract as well as HRLC-CMS has provided the database of 200 compounds and only relevant like Neuraminic acid, Ginkogolide, Gabapentin, Khivorin, and Altretamine.

Table -1: IR Interpretation and comparison of Centella Asiatica with donepezil and Rivastigmine.

S/N	Absorption observed (cm ⁻¹) in Methanolic extract of CA	Methanolic extract of Donepezil	Methanolic extract of Rivastigmine	Assignment	Absorption expected(cm ⁻¹)
1	3425.82	3424.76	3384.2	-OH in alcohol & Phenols	-OH stretch
2	2922.15	2915.53	-	-CH ₃ & CH ₂ in aliphatic compounds	2990-2850 -CH antisym and sym stretching
3	2853.49	2851.88	-	Aldehyde -C-H	2900-2800
4	1736.26	1671.39	-	>C=O	1600-1900
5	1629.22	1639.56	1654.03	>C=O(Amide)	1680-1630
6	1437.36	1438.96	1424.49	-C=C	1400-1600
7	1374.42	1364.7		-S=O	1375-1300

PAPL



No.	Peak	Intensity	Corr. Intensity	Base (H)	Base (L)	Area	Corr. Area
1	552.63	69.238	6.029	560.35	535.27	3.372	0.419
2	606.64	69.11	1.504	618.21	602.78	2.336	0.075
3	632.68	67.869	4.544	639.43	623.03	2.543	0.245
4	779.28	67.166	1.793	803.39	776.38	3.561	-0.041
5	875.72	73.453	11.619	888.26	859.32	2.6	0.586
6	899.83	74.403	9.377	908.51	888.26	1.943	0.393
7	1036.78	61.303	6.196	1047.39	1024.25	4.516	0.556
8	1071.5	61.968	2.944	1079.22	1063.79	3.06	0.166
9	1084.04	62.887	1.09	1086.93	1080.18	1.331	0.028
10	1093.69	61.533	3.728	1105.26	1087.9	3.384	0.241
11	1141.91	66.547	2.9	1154.45	1137.09	2.759	0.14
12	1167.95	68.733	7.4	1185.31	1154.45	4.146	0.546
13	1201.7	73.747	5.465	1212.31	1189.17	2.654	0.312
14	1201.7	73.747	5.465	1212.31	1189.17	2.654	0.312
15	1260.54	73.517	4.238	1271.14	1246.07	2.988	0.245
16	1340.58	69.187	5.236	1352.16	1328.05	3.399	0.303
17	1340.58	69.187	5.236	1352.16	1328.05	3.399	0.303
18	1424.49	69.547	1.527	1429.31	1422.56	1.024	0.025
19	1546.01	82.814	1.172	1548.91	1544.08	0.373	0.013
20	1654.03	79.337	6.856	1661.75	1653.07	0.735	0.128
21	3237.66	62.757	0.226	3239.59	3234.76	0.972	0.005
22	3259.84	62.236	0.276	3261.77	3255.02	1.375	0.007
23	3278.16	61.902	0.426	3280.09	3273.34	1.395	0.008
24	3286.84	62.036	0.33	3290.7	3282.99	1.591	0.008
25	3293.59	61.962	0.415	3296.49	3291.67	0.995	0.007
26	3298.42	62.033	0.173	3303.24	3297.45	1.196	0.004
27	3363.03	62.072	0.211	3364.96	3360.14	0.996	0.004
28	3379.43	62.008	0.3	3382.32	3377.5	0.996	0.006
Rivastigmine Tablet	3391	62.279	0.167	3391	3383.29	1.575	0.013

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Fig: 1 IR Spectra and Interpretation of Donepezil

Fig: 2 IR Spectra and Interpretation of Rivastigmine

Results and Discussion:

Various functional groups were analyzed by an IR spectroscopy like -OH in alcohol / phenols at 3425.82 cm^{-1} , aliphatic-CH₃ at 2922.1 cm^{-1} , aldehydic -CH at 2853.49 cm^{-1} , >C=O group at 1736.26 cm^{-1} , -C=O(Amide) at 1629.22 cm^{-1} , -C=C at 1437.36 cm^{-1} , -S=O at 1374.2 cm^{-1} , -C-N at 1322 cm^{-1} , -F at 1245.18 cm^{-1} , Aryl ether at 1055.34 cm^{-1} , and

Cl at 779.4 cm^{-1} , etc where when we examine the structures of drugs used for the treatment of AD are acetylcholine inhibitors like Galantmine, Donepezil and Rivastigmine¹³. The drugs like Donepezil shows the common functional groups like -OH in alcohol / phenols at 3424.76 cm^{-1} , aliphatic-CH₃ at 2941.57 cm^{-1} , aldehydic -CH at 2860.49 cm^{-1} , >C=O group at 1736.26 cm^{-1} , -C=O(Amide) at 1639.56 cm^{-1} , -C=C at 1438.96 cm^{-1} , -S=O at 1374.2 cm^{-1} , -C-N at 1305.86 cm^{-1} , -F at 1227.18 cm^{-1} , Aryl ether at 1060.89 cm^{-1} , and Cl at 887.29 cm^{-1} , and Rivastigmine shows the presence of similar functional groups like 3384.25 cm^{-1} , aliphatic-CH₃ at 2900 cm^{-1} , >C=O group at 1654.03 cm^{-1} , -C=O(Amide) at 1736.26 cm^{-1} , -C=C at 1424.49 cm^{-1} , -C-N at 1340.58 cm^{-1} , -F at 1260.54 cm^{-1} , Aryl ether at 1071.54 cm^{-1} , and Cl at 899.83 cm^{-1} , These are commonly employed acetylcholine inhibitor. Galanthamine is phenanthrine alkaloid having amide linkages, phenolic-OH, and also synthesized by using oxidative phenolic coupling¹⁴. Rivastigmine is a carbamate derivative and is related to Phosphohigmine and having Central Nervous system selectivity over peripheral inhibition¹⁵. Donepezil structure shows the presence of protein linkages, benzyl group, and aromatic hydrogen bond and having nitrogen interaction¹⁶. All these mentioned drugs are used as acetylcholine inhibitors but also reported to have few side effects and having the barriers about their supply of doses and can have limited efficacy, inconvenience. The respective investigation suggests that the plant is rich source of phytochemicals and medicinally active compounds, various functional groups observed are also the main part of various drugs.

Conclusion:

Electronic survey suggests that these drugs have certain barrier and side effects on human body so it's a suggestive and simple way through the study of Centella Asiatica where the result indicates that Centella Asiatica could be the a source of natural medicines for the treatment of Alzheimer's Disease. It can be a huge platform to investigate the plant further and the techniques which are reliable and safe for the synthesis of drugs. Naturally occurring phytochemicals may be less toxic than synthetic drug and natural extracts obtained from medicinal plants are concerned with certain specific medicinal effects, reproducibility and mechanism of action¹⁷. Various studies, articles also provide the evidence that Centella Asiatica has the mechanism action of reverent Alzheimer's Disease therapeutic and nueroprotective effects (Lee et al 2000)¹⁸. It can be a good source of natural medicines as the results show much of phytochemicals and a the plant is good source of medicinal values. There are numerous drugs available in western medicine that have been directly isolated from the plants or derived from the templates of compounds from the plants e.g. alkaloids from plant source

have been investigated for their potential in Alzheimer's Disease therapy¹⁹. The analysis of Centella Asiatica also shows the presence of alkaloids, so it will be of great interest to study further.

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