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Neurodegeneration-protective and rejuvenating properties of *Hydrocotyl asiatica* with evaluation of its essential micro-nutrient content.

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***Abstract*-Neurodegenerative diseases are characterized by progressive neuronal disorders and loss of neurons from specific regions of the brain. Though current research using synthetic chemical drugs is progressively going on to prevent, retard or reverse such neuro-degenerations, there is a tremendous scope to identify and study in this regard – isolating phytocompounds from herbal sources. In the present study ayurvedic 'Medhya Rasayana' herb *Hydrocotyl asiatica* (Mandukparni, Thankuni) has been selected. Different phytocompounds present in this herb are preliminary screened for the purpose using bioinformatic parameters (*in-silico*). Also essential micronutrient contents of the whole herb were determined using Atomic Absorption Spectrophotometer (AAS).**

***Keywords:* Neuro-degeneration, *Hydrocotyl asiatica*, Bioinformatics, biogeochemistry, micronutrient contents**

I. INTRODUCTION

Hydrocotyle asiatica (Syn. *Centella asiatica*, family *Umbelliferae*) is an important medicinal herb that has been used as a medicine in the Ayurvedic tradition of India for thousands of years and listed in the historic '*Atharva veda', 'Sushruta Samhita'* & *'Charaka Samhita'*. It has been used in Indian System of Medicine (as Medhya Rasayana) – improver of memory & nervous disorders, tonic and also in skin diseases, leprosy. Besides its common use as a medicinal plant, it is used fresh in salad and blended as a drink. It is also used in nutraceutical preparations, thus becoming an important rejuvenating herb.

In earlier studies, Appa Rao *et. al.* 1973 [1] showed the beneficial effect of Mandukparni (H. asiatica) on the general mental ability of mentally retarded children. Singh, Shukla & Mishra, 1981 [2] reported that a six week treatment with H. asiatica provided a significant relief in symptoms of anxiety neurosis leading to improved mental functions. Singh, Joshi & Vasavada, 1983 [3] reported the role of this herb in the management of some common health problems of aged. Agrawal SS, 1981 [4] reported anti-psychotic action of concentrated alcoholic extract of H. asiatica comparable to established drug, chloropromazine. However it showed varying degree of sedation in higher doses.

In vivo studies by Qi FY, *et. al.* 2014 [5], stated the neuro-protective property of asiaticoside wherein they demonstrated that asiaticoside could attenuate neurobehavioral, neurochemical and histological changes in transient focal middle cerebral artery occlusion animals and studies by Jung IM *et. al.*, 1999 [6], suggested the protective effects of asiaticoside derivatives against beta-amyloid neurotoxicity.

AMPA & SNCA receptors

Dementia is a type of neuro-degenerative disorder of the Central Nervous System wherein death of dopamine-generating cells in the midbrain are seen [7]. It includes disorders of speech, cognition, mood, behavior and thought. Behavior and mood alterations are more common with or without cognitive impairment, including impulsive control behaviors such as overuse of medication, craving, binge eating, hypersexuality or pathological gambling can be seen. Mutations in the SNCA (α-synuclein) receptor and AMPA (α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid) receptor are noted as causal factors [8, 9]. In our study the phytocompounds from H. asiatica was screened against the SNCA & AMPA receptors.

The α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor (also known as AMPA receptor, AMPAR, or quisqualate receptor) is a non-NMDA-type ionotropic transmembrane receptor for glutamate that mediates fast synaptic transmission in the central nervous system (CNS). AMPA receptors are responsible for the bulk of fast excitatory synaptic transmission throughout the CNS and their modulation is the ultimate mechanism that underlies much of the plasticity of excitory transmission that is expressed in the brain [10, 11, 12]. SNCA (Alpha-synuclein) is a member of the synuclein family, which also includes beta- and gamma-synuclein. SNCA may serve to integrate pre-synaptic signaling and membrane trafficking. Defects in SNCA have been implicated in the pathogenesis of Parkinson disease. SNCA peptides are a major component of amyloid plaques in the brains of patients with Alzheimer's disease. The release of neurotransmitters relays signals between neurons and is critical for normal brain function. SNCA may also help regulate the release of dopamine, an important neurotransmitter that is critical for controlling the start and stop of voluntary and involuntary movements [13, 14, 15, 16].

Mineral concentrations of *Hydrocotyl asiatica*

There is difference in mineral accumulation (major and trace) from soil by different plant species or varieties. Medicinal properties of plants depend on their organic or inorganic active constituents or on the combined effects of both. In view of number of important reviews [17, 18] on the extraordinary role of some essential trace minerals in the biochemical functions of living organism, their utilities in human and animal nutrition – Satsang Herbal Research Laboratory had taken the study of biogeochemistry and bioinorganic aspects of different medicinal plants with special emphasis on their essential trace mineral contents [19, 20, 21]. Trace elements are very important constituents in plants, in the sense – they cannot be synthesized by living matter. Moreover the essential trace elements in herbal sources are easily assimilated in the human system without any risk of toxicity and hence known as micronutrients. The essential trace elements normally occur and function in living tissues in very low concentrations. They are usually expressed as micro-gram per gram or in ppm (parts per million). In human system some trace elements are an integral part of important physiological compounds. Most but all trace elements act primarily as catalysts or co-factors in different enzyme system in the cells, where they serve a wide range of functions. Enzymes are important biological catalysts controlling body chemistry. Iron (Fe), Copper (Cu), Zinc (Zn), Manganese (Mn), Cobalt (Co), Chromium (Cr) and Selenium (Se) are essential components of a hundred different enzymes and their deficiency may produce promptly various deficiency syndrome or diseases.

In the present study, mineral contents (major & trace) of H. asiatica were determined using Atomic Absorption Spectrophotometer (AAS) – taking special precaution at every step to avoid metallic contamination of any form. The experimental results were further compared with those of some common food items and its phytocompounds were docked *in-silico* with 3d structural models of the AMPA & SNCA receptors.

II. METHODOLOGY

Phyto-compound constituents of *Hydrocotyle asiatica* isolated are: asiaticoside, terminolic acid, madecassoside, madecassic acid, brahmic acid and asiatic acid [22, 23, 24]. The above phyto-compound constituents are virtually screened against the CNS receptor models AMPA & SNCA and the docking scores are noted.

Essential mineral contents (major & trace) are determined using AAS.

III. RESULTS & DISCUSSIONS

The AMPA & SNCA receptors were modeled using modeler software [25] and the best model of each receptor was selected using

Ramachandran Plot server [26] as per studies by Bagchi P, Anuradha M and Kar A, 2017 (Fig. 1, 2).

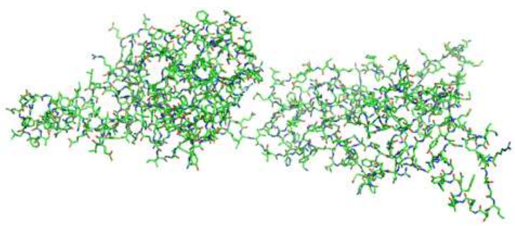


Fig. 1: 3d structure of AMPA receptor [27]

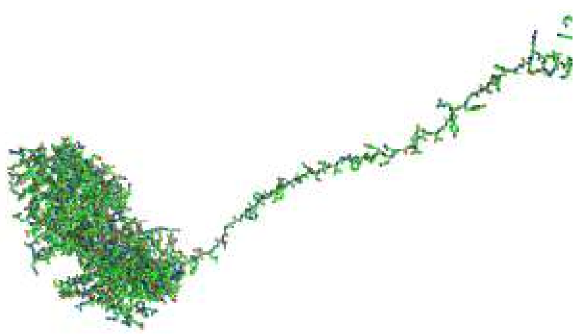


Fig. 2: 3d structure of SNCA receptor Model 4 [28]

The above receptors are docked with phytocompounds of H. asiatica and the docking scores are noted (Table 1, Fig. 3, 4).

Table 1: Docking results of AMPA & SNCA with phytocompounds

AMPA	Docking score (in -kcal/mol)	Interacting amino acid(s)
Asiaticoside	5658	Ser 5
Madecassoside	4968	Asn 177 Gly 178
Terminolic Acid	6058	Ala 93
Asiatic Acid	6020	Ala 93
Brahmic Acid	5788	Asn 190
Madecassic Acid	5788	Asn 190
SNCA		
Asiaticoside	5820	Gln 532
Terminolic Acid	6770	Tyr 420 Ala 412 Lys 299
Madecassoside	5122	Leu 350
Madecassic Acid	6430	Tyr 420 Gln 281
Brahmic Acid	6430	Tyr 420 Gln 281
Asiatic Acid	6308	Arg 392

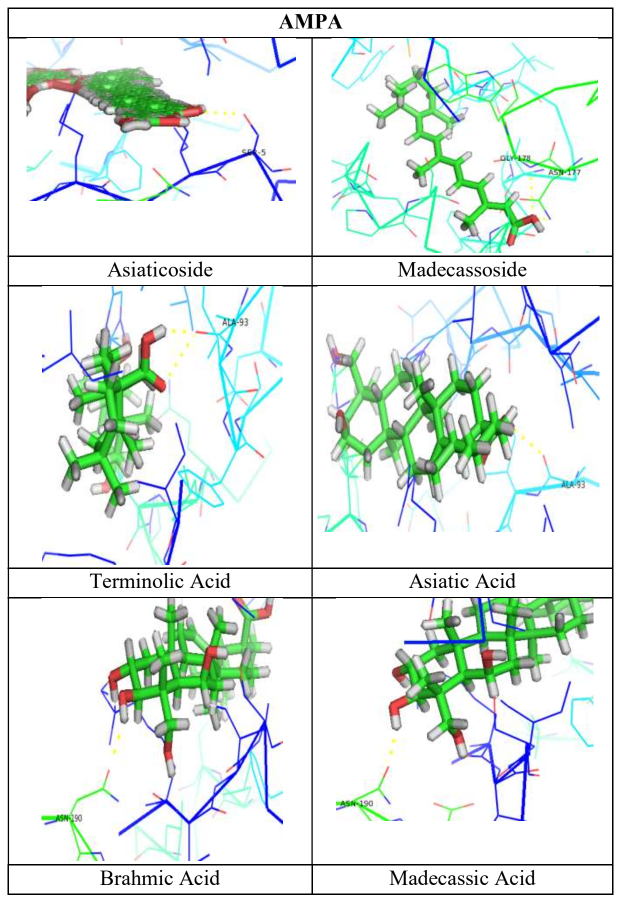
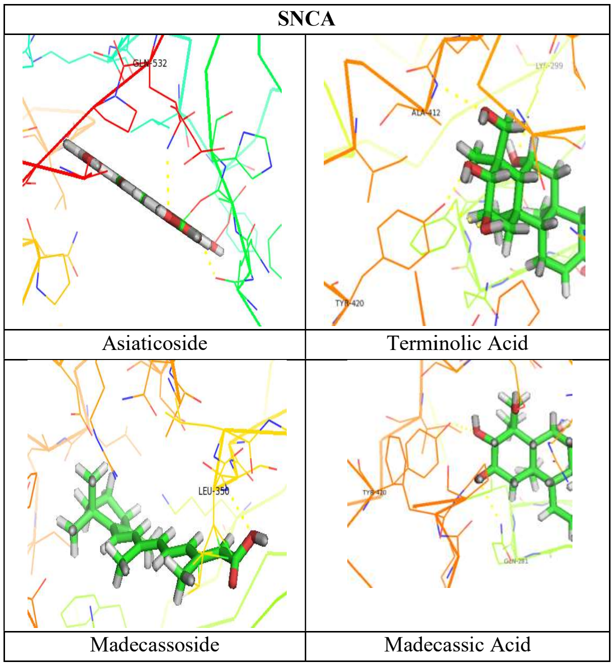


Fig. 3: Docking Results of AMPA With Phytocompounds



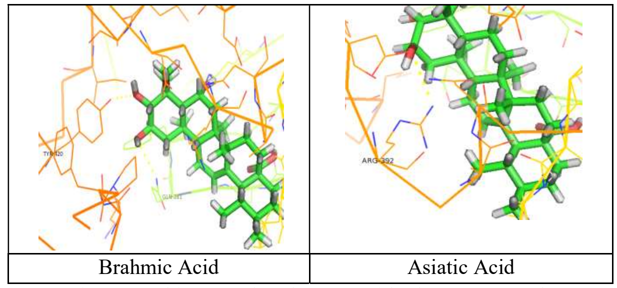


Fig. 4: Docking Results of SNCA with Phytocompounds

From Table 1 and Fig. 3 it is seen that the phyto-compounds have good interaction with AMPA & SNCA receptors suggesting that H. asiatica have good neuro-protective property.

Mineral contents of H. asiatica (major & trace) of the whole plant is reported in Table 2. Also, essential trace minerals (micro-nutrient) contents are compared with those of common food items listed in Table 2.

Table 2: Mineral contents of *Hydrocotyle asiatica*

	gm per 100 gm				Microgram per gram or ppm				
	Ca	Mg	K	Fe	Cu	Zn	Mn	Co	Cr
Hydrocotyle asiatica (whole plant)	1.83	0.53	3.80	0.26	2.81	61.10	61.60	9.44	1.80
Common food items									
Rice					4.10	6.50	2.80	0.16	0.16
Flour					1.50	3.50	5.20	0.36	0.23
Corn (Maize)					1.80	18.20	1.31	0.36	0.05
White sugar					0.57	0.20	0.13	0.05	0.02
Molasses					6.83	8.30	4.24	0.25	1.21
Milk					0.19	3.50	0.19	0.06	0.01
Butter					3.92	1.70	0.96	0.35	0.17
Egg					4.10	20.80	0.53	0.10	0.16
Tomato						0.60		0.06	0.01
Spinach						2.20	7.70	0.34	
Beet Root						0.50	0.41	0.06	

From Table 2 it is evident that the micro-nutrient contents Zinc (Zn), Manganese (Mn), Cobalt (Co), Copper (Cu) & Chromium (Cr) are present in significant concentration in this herb. As such regular use of H. asiatica in moderate dose justifies its rejuvenating property in human biochemical system.

REFERENCES

[1] Appa Rao, Srinivasan *et.al.*, 1973, Jour. Res. Ind. Med., 8(4): 9-16.

[2] Singh RH, Shukla SP & Mishra BC, 1981, Jour. Of Res. in Ayurv. & Siddha, 11(4): 1-10.

[3] Singh, Joshi & Vasavada, 1983, Med. & Aro. Plants Abst., 5(2): 164.

[4] Agrawal SS, 1981, Jour. Of Res. in Ayur. & Siddha, 11(11): 144-149.

[5] Qi FY, Yang L, Tian Z, Zhao MG, Liu SB, and An JZ, 2014, Neural Regen Res. 2014 Jul 1; 9(13): 1275–1282.

[6] Jung IM,Shin JE,Yun SH,Huh K,Koh JY,Park HK,Jew SS,and Jung MW, 1999, Journal of Neuroscience Research 58:417-425

[7] Alexander GE, 2004, Dialogues Clin Neurosci., 6(3):259–280.

[8] Klein C and Westenberger A, (2012), Cold Spring Harb Perspect Med., 2(1):1-15.

[9] Rachakonda V, Pan TH and Le WD, 2004, Cell Research, 14:347–358.

[10] Honore T, Lauridsen J, Krogsgaard-Larsen P, 1982, Journal of Neurochemistry. 38 (1): 173–178.

[11] Shi SH, Hayashi Y, Petralia RS, *et al.*, 1999, Science. 284 (5421): 1811–6.
[12] Mayer ML, 2005, Current Opinion in Neurobiology. 15 (3): 282–288.
[13] George JM, 2002, Genome Biol. 3 (1): REVIEWS3002.
[14] Polymeropoulos MH, Lavedan C, Leroy E, Ide SE, Dehejia A, Dutra A, *et al.*, 1997, Science. 276 (5321): 2045–7.
[15] Goedert M, July 2001, Nat. Rev. Neurosci. 2 (7): 492–501.
[16] Shah, M., Doctoral Thesis, 2013, The cytoskeletal linker protein, Ezrin, inhibits α-synuclein fibrillization and toxicity by a novel mechanism, Freien Universität Berlin.
[17] Mertz Walter, 1981, The Essential Trace Elements, Science, 213(18): 1331-1338.
[18] Roth H & Kirchgessner M, 1981, Bio. Trace Elements Res, 3:13-22.
[19] Kar A & Choudhary BK, 1994, Indian Drugs, 31(3): 127-130.
[20] Kar A, Choudhary BK & Bandyopadhyay NG, 1999, J. of Ethnopharmacology, 64(2): 179-184.
[21] Kar A, Choudhary BK & Bandyopadhyay NG, 2000, Adv. in Plant Sciences, 13(2): 413-421.
[22] Siddiqui BS , Aslam H , Ali ST , Khan S & Begum S, 2007, Journal of Asian Natural Products Research, 9(4):407-414.
[23] Gohil KJ, Patel JA, and Gajjar AK, 2010, Indian J Pharm Sci., 72(5): 546–556.
[24] Hashim P, Sidek H, Helan MHM, Sabery A, Palanisamy UD and Ilham M, 2011, Molecules 16:1310-1322.
[25] Sali A and Blundell TL, 1993, J. Mol. Biol., 234:779-815.
[26] Laskoswki RA, MacArthur MW, Moss DS & Thorton JM, 1993, J. Appl. Cryst. 26:283-291.
[27] Bagchi P, Anuradha M, Kar A, 2018, Neuropsychiatry, 8(3):1101–1114.
[28] Bagchi P, Anuradha M, Kar A, 2018, Information Systems Design and Intelligent Applications, Advances in Intelligent Systems and Computing 672, pp-1-9 by Springer Nature Singapore Pte Ltd.