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Molecular Pharmacology Of Antidepressive Terrestrial Natural Products (TNPs)

Mohit Kumar Sharma
Department of Pharmaceutical Sciences – Sardar Bhagwan Singh P.G. Institute of Biomedical Sciences & Research, Balawala, Dehradun, India
Prof. Veerma Ram
Department of Pharmaceutical Sciences – Sardar Bhagwan Singh P.G. Institute of Biomedical Sciences & Research, Balawala, Dehradun, India
Dr. Luv Kush
Department of Pharmaceutical Sciences – Sardar Bhagwan Singh P.G. Institute of Biomedical Sciences & Research, Balawala, Dehradun, India

Abstract:

Our new approach explored the phytopharmacotherapeutical significance of antidepressive TNPs through theoretical studies based on the antidepressant chemical structures.

Keywords: *Antidepressive, 5-HT (Serotonin), natural products, pharmacophoric, terrestrial.*

1.Introduction

Antidepressants have mood altering action. They improve depressive symptoms. The neurotransmitters like dopamine, norepinepherine and serotonin are implicated in the pathogenesis of the depression. They have sites of the action for the antidepressants. [4-6]

5-HT is happy neurohormone and implied in the depressive behavioral syndrome. The serotonergic receptor has prominence of transduction system and two sub-types (5-HT**1** and 5-HT**2**) of this receptor are related to antidepressive action. They are transmembrane domains G-protein linked. The pharmacophores of agonists, partial agonists and antagonists interacting with various 5-HT receptors generated the topographical information.[7-8-9]

Serotonin selective reuptake inhibitors (SSRIS)[8] selectively inhibit presynapic 5-HT uptake by enhancing serotonergic neurotransmission, thus prolonging serotonin duration of the action at the synapses. They have no affinity for muscarinic, histaminergic and adrenergic receptors.

2.Theoretical Methodology

The clinical depression is treatable by basic pharmacophoric moieties of antidepressive structures. They are feasible functionalities for binding with the active receptor surface[10-12,] It might provide possible mapping of the receptor surface for TNPs.

The antidepressive pharmacophoric moieties of eight potent TNPs were identified (Table-1). They have steroidal , alkaloidal, flavonoidal and napthodianthronal types of structures.

Sr. No.	**Compounds**	**Hetero atoms**		**No. of alkyl groups**	**Functionalities of heteroatom**	**Dose**
		Number	Nature			
1	Anhyperforin[13-19]	4	Oxygen	11	Ketonic, Alcoholic	1-10 mg/kg i.p.
2	Curcumin[21]	6	Oxygen	2	Phenolic, Ketonic	20-80 mg/kg oral

Sr. No.	**Compounds**	**Hetero atoms**	**No. of alkyl groups**	**Functionalities of heteroatom**	**Dose**	100 mg/kg s.c.
4	Hyperforin[13-19]	4	Oxygen	10	Ketonic, Alcoholic	1-10 mg/kg i.p.
5	Luteolin[21]	6	Oxygen	None	Ketonic, Alcoholic	10 mg/kg i.p.
6	Protopanaxadiol[23-24]	4	Oxygen	8	Alcoholic	0.2 mg/kg caudal vein
7	Santalol[2]	1	Oxygen	3	Alcoholic	25 mg/kg i.p.
8	Withinolides[26]	6	Oxygen	2	Alcoholic, Etheral, Ketonic	12.5-50 mg/kg oral

Table 1: The pharmacophoric moieties of the selected antidepressive TNPs

3.Results And Discussion

The role of pharmacophoric moieties was rationalized by looking at the reported data of dose/kg irrespective of mode of administration Anhyperforin and Hyperforin (1-10 mg/kg I.P) and Proyopanoxadiol (0.2 mg/kg caudal) have alkyl group between 8-11 range which may be contributing to their better hydrophobicity for crossing blood brain barrier in an effective manner. Curcumin (20-80 mg/kg orally), Luteolin (10mg/kg), Ginkgolide B (100 mg/kg S.C.) and Withianolides (12.5, 25, 50 mg/kg I.P.) have heteroatoms for H-bonding between 6-10 range therefore their better activity is attributed to extensive binding sites at receptor surface.

Topographical model of 5-HT is made of four binding sites. They are

- Aromatic site
- Hydrophobic site

- Positive ionizable site
- H-bond acceptor site

The majority of TNPs have structural rigidity by the virtue of ring fusions and pi-bonds. The nature of pharmacophore for TNPs has lipophilic sites for accommodating small alkyl groups and H-bond acceptor and donor sites for heteroatoms binding. The protonated nitrogen of TNPs interacts with anionic site through electrostatic or ionic binding.

4.Conclusion

The antidepressive receptor surface for TNPs should have binding sites for heteroatoms, hydrophobic groups and cationic groups which exhibited optimal pharmacophoric compliance with topographical surface of happy hormone. At molecular level, antidepressive action of TNPs can be attributed to the proposed topographical script.

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6.Reference

1. Cott. J, Mishra R. Medicinal Plant: a potential source for new psychotherapeutic drug, In: Kanba S et al., eds, New drug development from herbal medicines in neuropsychopharmacology, New York, Burnner/Mazel, Inc., (1997)
2. A selection of Prime Ayurvedic Plant Drugs (Ancient-modern concordance), Sukh Dev, Anamaya Publisher, F-154/2, Lado Sarai, New Delhi, (2006).
3. File://\ \1248161a-3\d\alok11_files\Effective() Natural Treatment for Depression. Html
4. Burger's Medicinal Chemistry and Drug Discovery sixth Edition, Volume 6: Nervous System Agent Edited by Donald J. Abraham ISBN 0-471-27401-1 @ (2003) John Wiley & Sons, Inc.
5. Surendra Nath Panday, a text book of Medicinal Chemistry (system and Biochemistry approach) Volume 3rd edition (2004) 212-528.
6. M.H. Lader in S.Checkly, Ed., The management of Depression, Blackwell Press, Oxford, UK, (1998), pp-118-211.
7. P.R. Hartig, in Serotonergic Neurons and 5-HT Receptors in the CNS (eds H. Baumgarten and M. Gohtert), Supringer-Verlag, New York, N.Y., (1997), Vol. 129, p. 175.
8. Devid A. Williams, Thomas L. L. mke Foye's Principle of Medicinal chemistry 5th edition (1974) reprinted (2002).
9. Selective 5-HT receptor modulators were last reviewed in 2000: A.J. Robinchaud and B.L. Largent, Annu. Rep. Med. Chem. (2000), 11, 35.
10. Corwin Hanch, comprehencsive Medicinal Chemistry, Voll.-1, Page 249, 274, 207 and Voll.-2 Page-125. First printed in India (2005).
11. Corwin Hanch, comprehencsive Medicinal Chemistry, Voll.-3, Page-567-597. First Printed in India (2005).
12. A. Karolkovas, "Essential of Molecular Pharmacology", wiley – Interscien New Your, (1970).
13. Chartterjee SS. Bhattacharya SK, Wonnemann M, Singer A, Muller WE. Hyperforin as a possible antidepressant component of Hypericum extracts. Life sci. (1998); 63:499-510.
14. Okpanyi SN, Weischer ML. Tierexperimentelle Untersuchungen zur psychotropen Wirksamkeit eines Hypericum-Extraktes. Arzneimittel-Forschung, (1987), 37:10-13.

15. Ozturk Y et al. Effects of Hypericum perforatum L. and Hypericum calycinum L. extract on the central nervous system in mice. Phytomedicine (9-1998), 63: 499-510.
16. Dimpfel W et al. Effects of a methanolic extract and a hyperforin-enriched CO_2 extracts of St John's wort (Hypericum perforatum) on intracerebral field potentials in the freely moving rat. Pharmacopsychiatry, (1998), 31 (Suppl. 1): S30-S35.
17. Butterwek V et. al. Effects of the total extract and fractions of hypericum perforamum in aminal assays for antidepressant activity. Pharmacopsychiatry, (1997), 30: 117-124.
18. Muller WE Rossol R. Effects of Hypercium extract on the expression of serotonin receptors. Journal of Genatric Psychiary and Neurology, (1994), 7 (Suppl. 1): receptors, Journal of Geriatric Psychiatry and Neurology, (1994), 7 (Suppl. 1): S63 S64.
19. Neary T, Bu YR. Hypericum Ll 160 inhibits uptake of serotonin and noepinephrine in astrocytes, Brain Research, (1999), 816.
20. Z.F. Yu, L.D Kong, Y. Chen, J Ethnopharmacol, 83, 161 (2002). R.H. Singh, J. Res. Ayur. Siddha, (1980)1, 133.
21. R.H. Singh, J. Res. Ayur. Soddha. 1, 133 (1980)
22. Hyeun Wook Chang. Biopharm. Bull. 28(12), 2181-2184 (2005)
23. http://www.umaso.edu/ansh/faq/htm.
24. http://www.ltmonline.org/arts/ginseng.htm
25. www/chemweb.com/journaltype=096894xsiid00150004
26. S.K. Bhattacharya, A. Bhattacharya, K. Sairam, S. Ghosal. Phytomedicine 7, 463(2000)