

Ayurvedic And Revolutionary Treatment In Schizophrenia

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I. INTRODUCTION

Schizophrenia is a perplexing, persistent emotional well-being jumble described by a variety of side effects, including dreams, fantasies, muddled discourse or conduct, and hindered intellectual capacity. The beginning stage of the illness, along with its persistent course, make it a debilitating problem for some patients and their families.^[1] Schizophrenia can be a weakening mental issue, with most of patients encountering critical comorbidity throughout their ailment. Studies have revealed intellectual and psychosocial deficiencies as of now at the beginning of disease.^[2] Schizophrenia is an incapacitating dysfunctional behaviour that influences 1% of the populace in all cultures.^[3] It is currently generally recognized that schizophrenia contributes generously to the worldwide weight of disease.^[4] It is additionally notable that schizophrenia is related with raised Self-destruction rates.^[5] World Health Organization characterizes schizophrenia as a extreme mental issue, portrayed by disturbed reasoning, influencing discernment, and language. It regularly incorporates crazy encounters, like hearing voices or delusions.^[6]

II. SYMPTOMS

1) Positive Symptoms

Positive manifestations can be effectively recognized and can be delegated insane practices not seen in sound individuals. Such manifestations incorporate pipedreams, daydreams, and strange engine conduct in fluctuating levels of severity.^[7]

2) Negative symptoms

Negative manifestations are somewhat hard to analyse and are related with high bleakness since they upset the patient's feelings and behaviour.^[8] The most widely recognized negative indications are a volition (Powerlessness to start and continue in exercises), logia (relative non attendance of Speech), anhedonia (absence of delight) and reduced passionate articulation.^[9]

Negative manifestations might be either essential to a finding of schizophrenia or auxiliary to drug, or natural factor an associative insane conclusion.^[10]

III. COMMON SUB-TYPES OF SCHIZOPHRENIA

1. Paranoid: Delusions or fantasies are conspicuous.
2. Hebephrenic:
 - a. Supported smoothed or indiscernible effect.
 - b. Absence of objective coordinated conduct
 - c. Noticeable idea disorder
3. Catatonic:
 - a. Supported proof over something like fourteen days of mental conduct including daze, fervour, posing, and unbending nature.
 - b. Straightforward Considerable loss of individual drive
 - c. Reformist extending of negative side effects
 - d. Articulated decrease in friendly, scholastic, or business performance.^[11]

IV. CAUSES OF SCHIZOPHRENIA

We will initially talk about the potential reasons for schizophrenia indications and how realizing them can prompt an effective comprehensive administration of the issue. There is no single reason of schizophrenia however a few components have been identified.^[12] As referenced over, the likelihood of creating schizophrenia was observed to be bigger in guys than females.^{[13][14]} Several investigations have shown that schizophrenia might be hereditary.^[15] It has been discovered that in the event that one of the guardians' experiences schizophrenia, the kids have a 10% shot at having that condition. People with schizophrenia may become touchy to any family strain, which might cause relapse.^[16] Alcohol and medication use, especially cannabis and amphetamine, may start psychosis in individuals helpless to schizophrenia.^{[17][18]} Individuals with schizophrenia use liquor also, different medications more than the general population.^[19]

V. PATHOPHYSIOLOGY OF SCHIZOPHRENIA

A few cerebra imaging and neuro-neurotic examinations have attempted to relate the indications of schizophrenia to various construction or capacity of explicit mind areas and circuits. There has been progression in associating a few parts of the issue to specific fundamental neurobiology and various lines of proof partner the support of the prefrontal cortex, inexplicit the intellectual deficiencies (for instance working memory and chief control)^[20]

In any case, sensitive decreases in dark matter and anomalies of white matter have been found across numerous cerebrum regions and circuits. The diminishing of dark matter advances with the time of ailment, especially in the transient projection, and is by all accounts related with antipsychotic treatment. Alternately, even medication credulous patients show volume diminishes (albeit not as articulated as treated patients), solely in the caudate core and halamus.

Besides, regardless of a huge number of studies, no confined physical or practical irregularities have been distinguished that are explicit to the problem. This is relied upon to mirror the trouble and heterogeneity of the psychopathology also, related intellectual insufficiencies, and the absence of clear edges isolating schizophrenia from the other disorders.^[20]

VI. DIAGNOSIS OF SCHIZOPHRENIA

Before 1980 the writing on early onset schizophrenia regularly portrayed indicatively heterogeneous gatherings of patients, since "youth schizophrenia" included patients who today would be analysed as having an insane issue? other than schizophrenia, or medically introverted or unavoidable formative problems. Nonetheless, a few analysts, for example, Kanner(1949) and Rutter (1972), respected mental imbalance and schizophrenia as two unmistakable entities.^[21] In case indications are available, your primary care physician will play out a complete clinical history and actual assessment. Despite the fact that there are no research centre tests to explicitly analyse schizophrenia, the specialist may utilize different symptomatic tests — for example, MRI or CT sweeps or blood tests — to preclude physical sickness as the reason for your symptoms.^[22] Determination of schizophrenia includes precluding other mental wellbeing problems and confirming that indications are not due to substance misuse, drug or an ailment. Deciding an analysis of schizophrenia might include:

- **Physical test.** This might be never really precluded different issues that could be causing side effects and to check for any connected intricacies.
- **Tests and screenings.** These might incorporate tests that assist preclude conditions with comparative indications, and evaluating for liquor and medications. The specialist may likewise demand imaging contemplates, for example, an MRI or CT check.
- **Psychiatric assessment.** A specialist or psychological well-being proficient actually looks at mental status by noticing appearance and disposition and getting some information about contemplations, dispositions, daydreams, mind flights, substance use, and potential for savagery or self-destruction. This moreover incorporates a conversation of family and individual history.
- **Diagnostic measures for schizophrenia** - A specialist or psychological well-being proficient may utilize the standards in the Symptomatic and Statistical Manual of Mental Disorders (DSM-5), distributed by the American Psychiatric Affiliation.^[23]
- **Blood tests** - in situations where medication use might be a factor a blood test might be requested. Blood tests are additionally done to prohibit actual reasons for ailment.
- **Imaging considers** - to preclude cancers and issues in the construction of the cerebrum.
- **Psychological assessment** - an expert will survey the patient's psychological state by getting some information about contemplations, states of mind, mental trips, self-destructive qualities, rough inclinations, or potential for brutality, just as noticing their attitude and appearance.^[24]

VII. TREATMENT ON SCHIZOPHRENIA

Schizophrenia requires profound established treatment, regardless, when appearances have faded away. Treatment with medications and psychosocial treatment can help with managing the condition. In a couple cases, hospitalization may be needed.^[23] Antipsychotic drugs have been the foundation of schizophrenia treatment since the introduction of chlorpromazine, focusing in on lessening the repeat and reality of insane scenes similarly as chipping away at the helpful constraint of individuals with schizophrenia.^[25]The destinations in treating schizophrenia consolidate zeroing in on signs, preventing lose the faith, and growing flexible working so that the patient can be composed again into the community.^[26] Pharmacotherapy is the foundation of schizophrenia the leaders, anyway extra signs may persevere. In this manner, no pharmacological meds, such psychotherapy, are similarly important.^[27]

VIII. ADVANCED TREATMENT ON SCHIZOPHRENIA

1) D2/D3 Partial Agonist-Cariprazine is a dopamine D3-liking, D3/D2 receptor half-way agonist. Its instrument of activity takes after the one showed by aripiprazole, yet cariprazine has stronger D3 adversary fractional agonist affinity.^[28] The D3 receptor is an auto receptor that seems to control the phasic? be that as it may, not tonic, action of dopamine, and it is for the most part circulated in limbic regions, the ventral striatum, and the thalamus.^[29]

2) Stepholidine-Stepholidine goes about as a D2 adversary, a D1 agonist, and a 5HT1A agonist and is being theorized as a medication viable in sure manifestations (Through the D2 receptor), just as in intellectual side effects (intensive the D1 and 5HT1A receptors).^[30] There is presently a continuous clinical preliminary being performed at the University of Toronto.^[31]

3) L-dopa-Based on the various affinities of dopamine receptors and on the allegedly, intellectual enhancer properties of the DA1 receptor, a clinical preliminary is being created to explore the possible impacts of certain portions of L-dopa as an increase treatment for negative/intellectual shortfalls of schizophrenia.^[19] A meta-investigation distributed in 2004 has recommended that adding L-dopa may be gainful for those patients previously taking antipsychotic medication.^[32]

4) YKP1358-YKP1358 is a D2/D3/5HT2A adversary that is at present going through stage 2 of clinical investigation (SKBio-Pharmaceuticals). Distributed examinations so far have explored the limiting properties of this medication on D2 receptors in the striatum.^[33]

5) Paliperidone-Paliperidone is the dynamic metabolite of risperidone and is accessible in oral and LAI details, both exhibiting efficacy and tolerability and a deferral on schedule to backslide in schizophrenia. It isn't hepatic ally utilized, making it protected to use in hepatic debilitation and with restricted danger of pharmacokinetic drug interactions.^[34] It can cause akathisia (expanded event at 10mgtwicedailydosingcomparedwith5mgtwicedaily), sedation and taste disturbance.^[35]

6) Lurasidone-Lurasidone is authorized for the treatment of schizophrenia.^[36] Lurasidone is for the most part well endured, with low rates of weight acquire and metabolic brokenness. It is related with akathisia (Expanded rate at dosages of 120mg or more noteworthy), sedation and queasiness, yet also to asenapine, regardless of been a full D2 adversary, it isn't

related with higher rates of EPSEs (excluding akathisia) what's more, hyperprolactinaemia.^[35]

7) Asenapine-Asenapine has exhibited adequacy in the intense and support periods of schizophrenia treatment and in the treatment of intense insanity in BPAD, yet it is just presently authorized for the treatment of insanity in the UK.

8) First-and second-age antipsychotics-More than 70 antipsychotics have been presented. They are fundamentally ordered into first-and second-age specialists and offer a comparable pharmacological component in hindering the dopamine D-2 receptors.^[37] Their obstructing instruments or activities are connected to their adequacy against positive and disorder side effects of schizophrenia.^[38-40] The original antipsychotics (FGAs), or commonplace antipsychotics (e.g., chlorpromazine, fluphenazine, and haloperidol, remembered for the World Health Organization's rundown of Fundamental Medications in 2009)^[41] were first presented for the treatment of schizophrenia during the 1950s... The second generation (abnormal) antipsychotics (e.g., clozapine, olanzapine, what's more, risperidone) presented over the most recent thirty years.

IX. HERBAL REMEDY OF SCHIZOPHRENIA

Regardless of being the standard treatment, antipsychotic drugs are related with numerous genuine antagonistic impacts. As indicated by WHO, very nearly 80 % of the complete populace of Africa and Asia depend on the regular natural cures. Regular natural drugs dependent on age old practice, viability and conviction have been broadly acknowledged in light of its lesser antagonistic impacts, demonstrated restorative worth against a ton of ailments, simple accessibility and agreeable cost tag.^[42-43] Spices have consistently managed the cost of significant leads against a number of afflictions and a few such home grown medications are advertised regularly.^[44] The plant based bioactive mixtures are fundamentally auxiliary metabolites utilized as home grown? therapeutics.^[45]

1. Aegle marmelos L. /Wood-apple or Bel (Rutaceae) Aegle marmelos, generally known as bel, stone apple or wood apple, is a tree indigenous to India and southeast Asia. The methanolic leaf concentrate of A. marmelos was allegedly applied enemy of tension and upper properties on pale skinned person mice and was additionally proposed as a plausible inventory for normal psychotherapeutic reagent.^[46]
2. Brassica juncea L. /Sorisha (Brassicaceae)- Brassica juncea, regularly known as green mustard or Indian mustard, is a specie of mustard plant. The plant is revealed for its relaxant movement. It is additionally

- accounted for decreasing the expanded thyroid movement in the schizophrenic patients.^[47]
3. Cannabis sativa L. /Siddhi (Cannabaceae) - Cannabis sativa, normally known as Ganja, Siddhi or Marijuana, is a yearly herbaceous plant having a place with the Cannabaceae family. The plant is known to have anxiolytic exercises and antipsychotic properties. Cannabidiol, a plant remove was referred to compelling in expanding tolerance and decreasing the olanzapine-produced unfriendly impacts in SZ patient.^[48]
 4. Matricariarecutita L. /Chamomile (Asteraceae) Chamomillarecutita, otherwise called chamomile or camomile, is a yearly plant of the family Asteraceae. Chamomile is a spice showing both unwinding and animating exercises. Its unstable oil extricate, contains bisobolol and chamazulene, announced for convulsive what's more, loosening up impact on CNS. It has been accounted for against anxious peevishness and anxiety.^[49]
 5. Hypericum perforatum L. /St.John'sWort (Hypericaceae)- Hypericum perforatum, ordinarily known as Saint John's wort (St John's wort), is a restorative spice with stimulant movement has a place with the family Hypericaceae. Concentrate of H. perforatum has been accounted for ketamine-offending impact. Sketamine astoundingly decreased the N100P200 top to top (ptp) adequacy after the fake treatment treatment.^[50]
 6. Wuling Powder (WLP)- Wuling powder (WLP), a wellrealized TCM is utilized in treating clozapine initiated hypersalivation, for the most part in youngsters. This customary home grown drug was first detailed from Han Line. It is figured by the combination of five Chinese natural extractions, those are Zhuling (Polyporus), Fuling (Poria), Zexie (Rhizomaalismatic). WLP diminished the hypersalivation essentially prompted by clozapine.^[51]
 7. Baicalin-Baicalin is a flavonoid (IUPAC name: 2S,3S,4S,5R,6S)-6-(5,6-dihydroxy-4-oxo-2-phenylchromen-7-yl)oxy-3,4,5-trihydroxy-tetrahydropyran-2- carboxylic corrosive; atomic equation: C₂₁H₁₈O₁₁) found in numerous species in the sort of Scutellaria, counting Scutellariabaicalensis, Scutellarialateriflora what's more, Scutellariagalericulata; family Lamiaceae. Baicalin was allegedly had prolyl oligopeptidase inhibitory capacity and has been accounted for to repress prolyl oligopeptidase. It was accounted for being likely contender to foster new antipsychotic drugs for SZ like neuropsychiatric disorders.^[52]

8. Ginkgo-Ginkgo trees (Ginkgo biloba) are local to East Asia and are filled decoratively in Europe and North America. Utilized in China for more than 2,000 a long time as a tea for treatment of asthma, ginkgo is currently the most regularly sold natural item in Germany also, one of the main three herbals in the United States, where it is taken basically to forestall or treat memory problems.^{[53][54]}

REFERENCES

- [1] Schizophrenia: Overview and Treatment Options, Krishna R. Patel, PharmD, RPh, Jessica Cherian, PharmD, RPh, Kunj Gohil, PharmD, RPh, and Dylan Atkinson
- [2] Bilder, Robert & Goldman, R.S. & Robinson, D & Reiter, G & Bell, L & Bates, J.A. &Pappadopulos, Elizabeth &Willson, D.F. &Alvir, J. &Woerner, M.G. & Geisler, S & Kane, J.M. & Lieberman, Jeffrey. (2000). Neuropsychology of first-episode schizophrenia: Initial characterization and clinical correlates. The American journal of psychiatry. 157. 549-59.
- [3] STEPHEN H. SCHULTZ, MD, STEPHEN W. NORTH, MD, MPH, and CLEVELAND G. SHIELDS, PhD, University of Rochester School of Medicine and Dentistry, Rochester, New York Am Fam Physician. 2007 Jun 15; 75(12):1821- 1829.
- [4] Murray CJLopez AD Global mortality, disability, and the contribution of risk factors: Global Burden of Disease Study. Lancet 1997; 349 (9063) 1436- 1442
- [5] Murray CJLopez AD Mortality by cause for eight regions of the world: Global Burden of Disease Study. Lancet 1997;349 (9061) 1269- 1276
- [6] Allebeck P. Schizophrenia: A life-shortening disease. Schizophr Bull. 1989;15:81-89
- [7] Grover, Sandeep &Davuluri, Triveni&Chakrabarti, Subho. (2014). Religion, Spirituality, and Schizophrenia: A Review. Indian journal of psychological medicine. 36. 119-124. 10.4103/0253-7176.130962.
- [8] Bucci, Paola &Galderisi, Silvana. (2017). Categorizing and assessing negative symptoms. Current Opinion in Psychiatry. 30. 1. 10.1097/YCO.0000000000000322.
- [9] Tandon, Rajiv & Nasrallah, Henry &Keshavan, Matcheri. (2009). Schizophrenia, "just the facts" 4. Clinical features and conceptualization. Schizophrenia research. 110. 1-23. 10.1016/j.schres.2009.03.005.
- [10] Research & Reviews: Journal of Nursing & Health Sciences,Schizophrenia: A General Review NishikantDoble.
- [11] Marco M Picchioni, clinical lecturer in psychiatry and Robin M Murray, professor of psychiatry.

- [12] Park S, Lee M, Furnham A, Jeon M, Ko YM. (2017). Lay beliefs about the causes and cures of schizophrenia. *Int J Soc Psychiatry*. 63:518–24. 10.1177/0020764017717283
- [13] Aleman A, Kahn RS, Selten JP. Sex differences in the risk of schizophrenia: evidence from meta-analysis. *Arch. Gen. Psychiatry* (2003) 60:565–71. 10.1001/archpsyc.60.6.565
- [14] McGrath JL, Saha S, Chant D, Welham J. Schizophrenia: a concise overview of incidence, prevalence, and mortality. *Epidemiol. Rev.* (2008) 30:67–76. 10.1093/epirev/mxn001
- [15] Matsumoto M, Walton NM, Yamada H, Kondo Y, Marek GJ, Tajinda K. The impact of genetics on future drug discovery in schizophrenia. *Expert Opin Drug Discov.* (2017) 18:1–14. 10.1080/17460441.2017.1324419
- [16] Buchanan WR. Persistent negative symptoms in schizophrenia: an overview. *Schizophr Bull.* (2007) 33:1013–22. 10.1093/schbul/sbl057
- [17] Nasrallah H, Hwang M. Psychiatric and physical comorbidity in schizophrenia. *Psychiatr. Clin.* (2009) 32:719–914. 10.1016/j.psc.2009.10.002
- [18] Pogue-Geile FM, Harrow M. Negative and positive symptoms in schizophrenia and depression: a follow-up, oxford journals, medicine and health. *Schizophr Bull.*(1984) 10:371–87.
- [19] Regier DA, Farmer ME, Rae DS, Locke BZ, Keith SJ, Judd LL, et al. (1990). Comorbidity of mental disorders with alcohol and other drug abuse. *JAMA* (1990) 264:2511–8.
- [20] Tamminga CA, Medoff DR(2002): Studies in schizophrenia: pathophysiology and treatment. *Dialogues ClinNeurosci.*, 4: 432-437.
- [21] Children with Schizophrenia: Diagnosis, Phenomenology, and Pharmacotherapy, by Elizabeth Kay Spencer and Magda Campbell, VOL. 20, NO. 4, 1994.
- [22] Stroup TS, Lawrence RE, Abbas AI, et al. The American Psychiatric Publishing Textbook of Psychiatry. Chapter 9. Schizophrenia Spectrum and Other Psychotic Disorders. American Psychiatric Publishing. Accessed 5/14/2018.
- [23] Patient Care & Health Information Diseases & Conditions, schizophrenia.(<https://www.mayoclinic.org/diseasesconditions/schizophrenia/diagnosis-treatment/drc20354449>)
- [24] Understanding the symptoms of schizophrenia, Last updated Thu 7 December 2017, By Christian Nordqvist .Reviewed by Timothy J. Legg, PhD, CRNP
- [25] DELAY J, LAINE B, BUISSON JF: Note concernant l'action de l'isonicotinyl-hydrazide utilisédans le traitement des états dépressifs. *Ann Med Psychol (Paris)* 1952, 110:689-92.
- [26] Crismon L, Argo TR, Buckley PF. Schizophrenia. In: DiPiro JT, Talbert RL, Yee GC, et al, eds. Pharmacotherapy: A Pathophysiologic Approach. 9th ed. New York, New York: McGraw-Hill; 2014:1019–1046.
- [27] Dickerson FB, Lehman AF. Evidence-based psychotherapy for schizophrenia: 2011 update. *J NervMent Dis* 2011;199(8):520–526.
- [28] Citrome L: Cariprazine in schizophrenia: clinical efficacy, tolerability, and place in therapy. *AdvTher* 2013; 30:114–126
- [29] George M, Amrutheshwar R, Rajkumar RP, et al: Newer antipsychotics and upcoming molecules for schizophrenia. *Eur J ClinPharmacol* 2013; 69:1497–1509
- [30] Guo Y, Zhang H, Chen X, et al: Evaluation of the antipsychotic effect of bi-acetylated 1-stepholidine (1-SPD-A): a novel dopamine and serotonin receptor dual ligand. *Schizophr Res* 2009; 115:41–49.
- [31] Mango D, Bonito-Oliva A, Ledonne A, et al: Phosphodiesterase 10A controls D1-mediated facilitation of GABA release from striato-nigral projections under normal and dopamine-depleted conditions. *Neuropharmacology* 2014; 76(pt A):127–136
- [32] Jaskiw GE, Popli A: A meta-analysis of the response to chronic l-dopa in patients with schizophrenia: therapeutic and heuristic implications. *Psychopharmacology (Berl)* 2004; 171:365–374.
- [33] Pharm The American Journal of Psychiatry Residents' Journal-pharmacological Advances in the Treatment of Schizophrenia by Javier Ballester, M.D. Brian A. Frankel, M.D.
- [34] Taylor D, Paton C, Kapur S. The Maudsley Prescribing Guidelines in Psychiatry. Wiley, 2012.
- [35] Citrome L. A review of the pharmacology, efficacy and tolerability of recently approved and upcoming oral antipsychotics: an evidence-based medicine approach. *CNS Drugs* 2013; 27:879–911.
- [36] Joint Formulary Committee. British National Formulary (BNF) 67. Pharmaceutical Press, 2014.
- [37] Kapur S, Remington G. Dopamine D(2) receptors and their role in atypical antipsychotic action: still necessary and may even be sufficient. *Biol Psychiatry*. 1 2001; 50(11):873–883
- [38] Patterson TL, Leeuwenkamp OR. Adjunctive psychosocial therapies for the treatment of schizophrenia. *Schizophr Res.* 2008; 100(1–3): 108–119.
- [39] Pfammatter M, Junghan UM, Brenner HD. Efficacy of psychological therapy in schizophrenia: conclusions from meta-analyses. *Schizophr Bull.* 2006; 32 Suppl 1: S64–S80.
- [40] Rector NA, Beck AT. Cognitive behavioral therapy for schizophrenia: an empirical review. *J NervMent Dis.* 2001; 189(5):278–287
- [41] World Health Organization. WHO Model List of Essential Medicines. 17th ed. Available

- from:http://www.who.int/medicines/publications/essential_medicines/en/index.html. Accessed June 18, 2013.
- [42] Dey, A., Nath De, J. (2012). Anti-snake Venom Botanicals Used by the Ethnic Groups of Purulia District, West Bengal, India. *Journal of Herbs, Spices & Medicinal Plants*, 18(2): 152-165.
- [43] Dey, A., De, J.N. (2012). Ethnomedicinal plants used by the tribals of Purulia district, West Bengal, India against gastrointestinal disorders. *J. Ethnopharmacol*, 143(1): 68-80.
- [44] Balunas, M.J., Kinghorn, A.D. (2005). Drug discovery from medicinal plants. *Life Sciences*, 78(5): 431-441.
- [45] Itokawa, H., Morris-Natschke, S.L., Akiyama, T., Lee, K.H. (2008). Plant-derived natural product research aimed at new drug discovery. *Journal of Natural Medicines*, 62(3): 263- 280.
- [46] Ahmed, M.N., Azam, K., Nur, M. (2014). Traditional knowledge and formulations of medicinal plants used by the traditional medical practitioners of Bangladesh to treat schizophrenia like psychosis. *Schizophrenia Research and Treatment*, 1-10.
- [47] Cranswick, E.H. (1955). Tracer iodine studies on thyroid activity and thyroid responsiveness in schizophrenia. *American Journal of Psychiatry*, 112(3): 170-178.
- [48] Zuardi, A.W., Hallak, J.E., Dursun, S.M., Morais, S.L., Sanches, R.F., Musty, R.E., Crippa, J.A.S. (2006). Cannabidiol monotherapy for treatment-resistant schizophrenia. *Journal of Psychopharmacology*, 20(5): 683- 686.
- [49] Cabrera, C. (1997). Nervous - Successful treatment of Schizophrenia with phytotherapy. *Medical Herbalism*.7 (3): 8- 15.
- [50] Murck, H., Spitznagel, H., Ploch, M., Seibel, K., Schaffler, K. (2006). Hypericum extract reverses S-ketamine-induced changes in auditory evoked potentials in humans—possible implications for the treatment of schizophrenia. *Biological Psychiatry*, 59(5): .440-445.
- [51] Hung, C.C., Fu, P.K., Wang, H.Y., Chan, C.H., Lan, T.H. (2011). Treatment effects of traditional Chinese medicines Suoquan Pill and Wuling Powder on clozapine-induced hypersalivation in patients with schizophrenia: study protocol of a randomized, placebo-controlled trial. *Zhong xi yijie he xuebao=Journal of Chinese Integrative Medicine*, 9(5): 495- 502.
- [52] Tarragó, T., Kichik, N., Claasen, B., Prades, R., Teixidó, M., Giralt, E. (2008). Baicalin, a prodrug able to reach the CNS, is a prolyl oligopeptidase inhibitor. *Bioorganic & Medicinal Chemistry*, 16(15): 7516-7524.
- [53] Singh YN, Effect of kava on neuromuscular transmission and muscle contractility, *Journal of Ethnopharmacology*, 7, 1983, 267-276.
- [54] HERBAL AND DIETARY SUPPLEMENTS IN TREATMENT OF SCHIZOPHRENIA: AN APPROACH TO IMPROVE THERAPEUTICS, Volume 10, Issue 1, September – October 2011; Article-035.