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RESEARCH ARTICLE

AN OVERVIEW OF THE INTERACTIONS BETWEEN AYURVEDIC HERBS AND PSYCHIATRIC DRUGS

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Abstract

Introduction: Ayurvedic drugs are used to treat various medical conditions, including psychiatric diseases (manasika vikaras). Increased awareness about Ayurvedic drugs along with easy availability has lead to the increase in self- medication for many health issues. One among them is the simultaneous intake of psychiatric drugs and herbal medications without any knowledge of the potential interactions between them. A drug interaction occurs when the effect of a drug is altered by the presence of other drugs, herbal supplements, or foods. Herb-Drug interactions are more common than Drug-Drug interactions because herbal medicines contain multiple pharmacological ingredients. Drug interactions between Ayurvedic medicinal herb and Psychiatric drugs can be either synergistic or antagonistic. This can lead to enhanced or diminished effect that may be useful or harmful. The search for drug interaction yields information predominantly pertaining to Western medicine, with limited content on Indian medicinal herbs, especially Ayurvedic medicines. The information of herbs and drugs interaction is incomplete or lacking in detail; they affect either the pharmacokinetic fates or pharmaco dynamics activities of drugs, leading to therapeutic failure or toxicities. Hence, this is a humble attempt from the pharmacovigilance perspective to review and create awareness regarding the possible interaction between Ayurvedic herbs and Psychiatric drugs.

Introduction:-

Ayurveda, also called as “Biological science medicine” is geared up to take its place as the mainstream of healthcare and witnessing a renaissance.[1] Ayurveda is a conglomeration of the four interdependent components namely, the body (Shareera), the sensory and motor faculties (Indriya), the mind (Satva), and the soul (Atma). Achieving health requires a harmonious balance among these elements, reflecting a comprehensive concept of well-being that encompasses the physical, mental, sensory, and spiritual dimensions. Ayurveda focuses on preserving and promoting health while preventing and treating diseases by emphasizing the principles of positive physical and mental well-being. The popularity and availability of herbal drugs among people has led to increase in self medication along with modern medicine. One of the essential prerequisites in achieving healthy body is healthy mind (Prasanna mana) which is emphasized in the context of Swastya (healthy state).[2] Body, mind, and soul are seen as a tripod, and their combination sustains the world. Together, they form the foundation for all existence. [3] Similarly, the body and mind serve as substratum for both disease and happiness.[4]However, when the mind (manas) is affected; medications are administered for mental ailments (manasikavyadhi).

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Manasika Vyadhisencompass a range of mental disorders, including Unmada (Insanity), Apasmara (Epilepsy), Grahabadha (Temper Tantrums), and Atatwabhinivesa (Delusional Disorder/Obsessive-Compulsive Disorder). These conditions are characterized by impairments in various mental functions such as consciousness, imagination, perception, thinking, intelligence, judgment, language, memory, and emotions. Ayurvedic psychotherapy focuses on managing mental disorders through the application of core Ayurvedic principles.[5] The specialized treatment of manasikaroga (Psychiatric disorders) held significant importance as one of eight branches of Ayurveda known as Ashtangas. Acharya Charaka emphasizes that the management of mental illnesses should be entrusted to a skilled expert specializing in the field.[6] Amarsha (irritation), Asthane Krodha (anger), Bhaya (fear), Udwega (anxiety), Thurshnibhavatwa (depressive mood) etc are the common conditions encountered in Ayurveda practice and for which various medical and spiritual therapies are advised.[7]

The COVID-19 outbreak has contributed to increase of various psychological issues and significant consequences on mental health, such as stress, anxiety, depression, frustration, and sleeplessness. The usage of antidepressants has witnessed a significant surge in the post-COVID era. The psychological effects of quarantine during the COVID-19 pandemic, along with the key psychological reactions observed in the general population during the outbreak, have been extensively documented together.[8] Physical distancing, which was recommended to "flatten the curve" encouraged to decelerate the rate of COVID-19 transmission within the general public resulted in loneliness for some individuals, particularly those living alone, including the elderly. Senior citizens over the age of 70, immune-compromised individuals, and those with chronic illnesses often face heightened levels of anxiety, depression, and worry. Critical illnesses and subsequent stays in intensive care units expose patients to severe physiological and psychological stressors, which are often life-threatening and traumatic, frequently leading to long-term psychiatric conditions.

The use of herbal products as complementary medicine is common among patients concurrently taking neuropsychiatric medications. Herb-drug interaction, a clinical consequence of this practice, may jeopardize the success of pharmacotherapy in neuropsychiatry.[9] Many patients seek psychotropic drugs such as barbiturates, benzodiazepines, and others to alleviate the aforementioned psychological issues. At the same time, many people opt for herbal remedies like Ashwagandha (Withania somnifera), Brahmi(Bacopa monneiri), Tulsi(Ocimum sanctum), and ginger (Zingiber officinale), alongside conventional allopathic psychiatric medications, as preventive self-care measures. The simultaneous use of herbs may either magnify, or counteract the effects of medications. However, many reports of herb-drug interactions remain unclear and often lack laboratory analysis of the involved preparations.[10] Currently, there is no comprehensive data available regarding potential interactions between herbs and modern psychiatric medications in a single source. For example, Brahmi (Bacopa monnieri) interacts with fluoxetine resulting in serotonine syndrome. Midazolam, a commonly prescribed anxiolytic medicine during COVID-19 treatment interacts with Aswagandha and amplifies its sedative effect.

Methodology:-

A comprehensive review of the literature on herb-drug interactions was done. Classical textbooks, research papers, bulletins, official websites were referred. The key words used during Google search were herb-drug interaction, psychiatric drug interaction.

instances of herb drug interaction:

1. Drug interaction involving Ashwagandha (Withaniasominifera) and Clonazepam, Diazepam, Lorazepam, Alprazolam (Benzodiazepines), Barbiturates. Benzodiazepines are a class of medications that slow down activity in the brain and nervous system and often used to treat anxiety disorders, as well as brain-related conditions like seizures. They appear to work by affecting neurotransmitters in the brain, chemicals that nerves release in order to communicate with other nearby nerves.

   Ashwagandha (Withaniasominifera) has an additive effect when it interacts with Benzodiazapine.[11] Ashwagandha when consumed along with sedative medications might cause too much sleepiness. Some of these sedative medications include Clonazepam (Klonopin), Diazepam (Valium), Lorazepam (Ativan), Alprazolam (Xanax), Flurazepam (Dalmane), Midazolam (Versed) and others.[12] It may potentiate the effects of barbiturates and sedatives when used simultaneously. The drug has additive effect when used in combination with diazepam. The combination when used in status epilepticus was able to reduce significantly the effective dose of diazepam and offer complete protection with no subsequent mortality.[13] Patients experiencing recent

exacerbation of schizophrenia show notable improvements in negative, general, and total symptoms, as well as reduced stress when treated with a standardized extract of Ashwagandha, with minimal associated side effects.[14]

2. Drug Interaction between Jatamamsi (Nardostachys jatamansi) and Benzodiazepines: Nardostachys jatamansi should be administered with caution in patients taking benzodiazepines or other sedative medications, as it may exhibit an additive sedative effect.[15]
3. Drug interaction involving Brahmi (Bacopa monnieri) and Fluoxetine, Haloperidol, Risperidone, Alprazolam, Zolpidem. Fluoxetine is a type of antidepressant known as a selective serotonin reuptake inhibitor (SSRI) which is often used to treat depressive disorders, obsessive compulsive disorder, bulimia, premenstrual dysphoric disorder, panic disorder.Extracts of Brahmi **(**Bacopa monnieri)inhibits CYP2C19, CYP2C9, CYP1A2, CYP3A4, patients taking B. monnieri with the antidepressant, antipsychotic, antiepileptic drugs could experience an increase in the plasma level of the drugs, resulting in significant adverse reactions or toxicities.[16]

a) The combination of Bacopa monnieri and Fluoxetine can lead to Serotonin Syndrome, a potentially life-threatening condition precipitated by the use of serotonergic drugs. This syndrome may result from therapeutic medication use, unintended drug interactions, recreational drug use, or intentional overdose.

b) Bacopa monnieri with Haloperidol results in urinary retention, SIADH (Syndrome of inappropriate antidiuretic hormone secretion) induced urinary retention.

c) Bacopa monnieri with Risperidone and chlorprothixene results in hyperhidrosis and salivation

d) Bacopa monnieri with Alprazolam – In Contrary to the popular belief that Bacopa enhances memory it may result in memory dysfunction and retrograde amnesia.

e) Bacopa monnieri with Zolpidem - Results in Amnesia.[17]

4. Drug interaction involving Mandukaparni (Centella asiatica) with sleep inducers / Anxiolytics - Anxiolytics are class of medications used to prevent or treat anxiety symptoms or disorders. Administration of high doses of Centella asiatica can cause sedation, since it should be avoided on patients who are on anxiolytics or tranquilizers.[18]
5. Drug interaction involving Shankhapushpi (Convolvulus pluricaulis) (CP) and Phenytoin.-Phenytoin is a hydantoin derivative, a first-generation anti-convulsant drug that is effective in the treatment of generalized tonic-clonic seizures, complex partial seizures, and status epilepticus without significantly impairing neurological function. CP can decrease concentrations of phenytoin, leading to decreased control of seizure. It has been shown that during multiple-dose co administration, CP reduced not only the antiepileptic activity of phenytoin but also lowered plasma phenytoin levels.[19] Convolvulus pluricaulis in combination with Omega-3-fatty acid gives significant anxiolytic effect.[20]
6. Drug interaction involving Grape fruit juice (Vitis vinifera) and Benzodiazepines. Consumption of grapefruit juice has increased the oral bioavailability of various drugs, including calcium channel blockers (e.g., Felodipine, Nifedipine), HMG-CoA reductase inhibitors (Simvastatin, Lovastatin), benzodiazepines (Midazolam, Triazolam)[21]. Furanocoumarins (paradisins, bergamotin) present in grapefruit juice modify the metabolism of Alprazolam and Felodipine by inhibiting the activity of CYP_{450} 3A4 and Pgp transporters in the gastrointestinal tract and liver.[22]
7. Drug interaction involving Tulasi (Ocimumtenuiflorum/sanctum) and Pentobarbital- Pentobarbital or pentobarbitone is a short-acting barbiturate typically used as a sedative, a pre anesthetic, and to control convulsions in emergencies. It can also be used for short-term treatment of insomnia. There is some concern that Ocimumtenuiflorum/sanctum seed oil when taken along with pentobarbital might cause too much drowsiness.[23]
8. Drug interaction involving Tagar (Valeriana officinalis/Valeriana Wallichi) and Alprazolam/Benzodiazepines-Consuming valerian with alprazolam might increase the effects and side effects of Alprazolam such as drowsiness. The maximum concentration of alprazolam in plasma was found to be significantly increased after treatment with valerian.[24] Hence, valerian might cause prolonged sedation when taken along with sedative medications which are used in surgery.
9. Drug interaction involving Shunti (Gingiber officinalis) and Sertraline/antidepressant drugs. Sertraline is an antidepressant of the selective serotonin reuptake inhibitor (SSRI) class of medications. It is used to manage and treat the major depressive disorder, obsessive-compulsive disorder, panic disorder, post-traumatic stress disorder, premenstrual dysphoric disorder, and social anxiety disorder.
   Gingiber officinalis has a neuroprotective effect by avoiding the side effects of the sertraline, an antidepressant drug.[25] The plant extract of Zingiber officinaleshowed significant antidepressant activity in forced swim test model and significant antinociceptive effect in acetic acid induced writhing.[26]

10. Drug interaction involving Satahwa/Anise (Pimpinella anisum) seeds/fruit and Benzodiazepines, Pentobarbital, Fluxetine, Imipramine. The sedative effects of the three drugs listed below were enhanced, even though Pimpinella anisum (Anise oil) by itself did not exhibit sedative properties.

a) The combination of Pimpinella anisum with codeine significantly enhances analgesic activity.
b) The combination of midazolam with Pimpinella anisum has led to greater motor impairment.
c) Pimpinella anisum (Anise oil) enhanced the effects of diazepam by further reducing motor activity.

On the other hand, Anise oil reduced the action of below 3 drugs.

a) Anise oil significantly shortened the sleeping time induced by pentobarbital.
b) Anise oil pretreatment reduced the antidepressant effects of fluoxetine and imipramine. These findings highlight the potential interactions of anise essential oil with drugs affecting the central nervous system, indicating that such combinations should be avoided in humans.[27]

Similarly, Diclofenac sodium (DIC) which is a widely used anti-inflammatory drug, if administered with herbal drugs containing piperine (PIP) like Pippali (Piper longum) Pepper (Piper nigrum) drug–phytochemical interactions occur.Altered pharmacokinetics of DIC might be attributed to piperine mediated inhibition of CYP2C9 enzyme, which indicates the clinically significant interaction present between DIC and PIP.[28]

Conclusion:-

Increased awareness about Ayurvedic medicines among the consumers have led to the concurrent use with allopathic medicines. There is a misconception among the people that "anything herbal is safe". Herb drug interactions are highly important in clinical practice since majority of the patients will be on allopathic medications. Pharmacokinetic or pharmacodynamics activities of drugs are altered leading to exaggerated or diminished effects. They may even lead to therapeutic failures. Hence, it becomes important to assess the clinical therapeutic efficacy. Concomitant use of Ayurvedic drugs along with antipsychotic drugs thus, acts as a confounding factor in diagnosing the adverse reaction. More documentation as well as studies involving insilico model is needed to confirm the potential herb-drug interactions. An updated knowledge regarding herb drug interactions is the need of the hour. This study gives a glimpse of possible drug interactions between Ayurvedic herbs with conventional psychiatric drugs. Dissemination of information with few examples quoted here intend to create awareness among Ayurveda physicians about the possible herb drug interactions. In future new tools like artificial intelligence may be used to predict the possible herb drug interactions and new strategies may be developed to prevent adverse drug reactions.

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Conflict Of Interest:

Authors declare that there is no conflict of interest.

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