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A Review on Depression- A Serious and Life -Threatening Problemin Present Time

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ABSTRACT-Depression is a severe mental health disorder characterized by persistent sadness, hopelessness, and a lack of interest in daily activities. It is a leading cause of disability worldwide and is influenced by genetic, neurobiological, and environmental factors. Dysregulation in neurotransmitter systems is a key factor. Antidepressants are the primary pharmacological treatment for moderate to severe depression, aiming to correct imbalances in brain chemistry. However, their mechanism of action is not fully understood, and individual responses vary. Common side effects include gastrointestinal disturbances, weight changes, sexual dysfunction, and increased suicidal thoughts, especially in younger populations. The effectiveness of antidepressants is often enhanced when combined with psychotherapy or other non-pharmacological treatments. Challenges remain in optimizing treatment strategies, as not all patients respond to first-line medications. Research is ongoing to understand depression's underlying mechanisms, develop targeted therapies, and identify predictors of treatment response. Despite these advancements, there is a growing recognition of the need for personalized, holistic approaches that address both biological and psychosocial components of depression. Ayurvedic treatment also plays a vital role in treatment of depression. Various herbs are used in ayurveda are Ashwagandha Brahmi guduchi etc. Homeopathic formulations also used in the treatment of depression proven by some studies.: Arsenic album, Aconite, Silica are the homeopathic products that plays a most vital role in the treatment of depression. Some physicians also suggest to take some Nutraceuticals and supplements for curing from depression such as Vitamin B6, Vitamin B9, calcium, magnesium and omega- 3S-.

Keywords
Here are some keywords from the article:
- Depression
- Mental health
- Antidepressants
- Neurotransmitters
- Serotonin
- Cognitive Behavioural Therapy (CBT)
- Ayurvedic treatment
- Homeopathy
- Nutraceuticals
- Vagus nerve stimulation
- Electroconvulsive therapy (ECT)
- Types of depression
- Clinical depression
- Vitamin B6, B9, B12
- Stress management
- Psychotherapy

I. INTRODUCTION-

Depression is the leading cause of disability worldwide, according to the "WHO"It can undermine a person's relationships, make working and maintaining good health very difficult, and in severe cases, may lead to suicide. In fact, depression contributes to nearly 40,000 suicides in the United States and 100000 in all world eachyear. It can affect adults, adolescents, and children. This article examines what depression is and what causes it, as well as types of depression, treatment, and more[1.]Depression is a common and serious mental disorder that negatively affects how you feel, think, act, and visualise the world.According to 2023 national1 survey about (29%) adults have been diagnosed with depression at some point in their lives and about 18% are currently experiencing depression.Women are more likely than men and younger adults are more likely than older adults to experience depression. While depression can occur at any time and at any age, on average it can first appear during ones late teens to mid 20sThere are several other treatments which are used in the treatment of depression such as ayurvedic, homeopathic etc.[2]

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1. Ayurvedic Treatment-

In Ayurveda, MDD is linked to Kaphaja Unmada in severe cases and Vichada and Vasavada in mild cases. In severe cases, Kapha Pradhan tridosha derangements occur, while in mild cases, Kapha vataja derangements are observed. Vishada is a vataja Nat AtmajaVicara, more prevalent in Hinna satwa purusha (decreased mental strength). Symptoms include avasada of manas, Vaak, and kaya, and the presence of Vishaka can aggravate co-existing disease conditions.[3]

(i) **Ashwagandha**- Also known as Indian ginseng. It plays important role in reducing stress conditions and also help to control mood swings.
(ii) **Brahmi**- It calms down the mind which helps in treating depression.
(iii) **Guduchi**- It also known as giloy and it also plays role in anxiety and depression conditions.
(iv) **Bhringaraj**- It is a herb that can control anxiety and stress.[4,5]

2. **Homeopathic Treatment-**

There are various homeopathic products which are used in treatment for depression.
(i) **Arsenic album**- It is a natural medicine to cure the extreme problem of stress.[6]
(ii) **Aconite**- This medicine can used to treat acute anxiety attacks.[7]
(iii) **Silica**- This can help those who have a lack of self-confidence and fear of public speaking.
(iv) **Passion flower**- It is more effective in treating anxiety and nervousness. [8]

Types of Depression

- **Clinical Depression-**A diagnosis of major depressive disorder means the patients feels sad, low for atlast two weeks while also having other symptoms such as sleep problems, loss of interest in activities or change in appetite.[9]

- **Persistent Depressive Disorder-** Persistent depressive disorder (PDD) is a mild or moderate depression lasting at least two years, with symptoms less severe than major depressive disorder, previously known as dysthymia.[10]

- **Disruptive mood dysregulation disorder-** Persistent depressive disorder is mild or moderate depression that lasts for at least two years. The symptoms are less severe than major depressive disorder. Healthcare providers used to call PDD dysthymia.[11]

- **Premenstrual dysphoric disorder-**PMDD is characterized by premenstrual syndrome symptoms and mood issues like irritability, anxiety, or depression, which typically improve within a few days post-menstruation but can still significantly impact life.[12]

- **Depressive disorder due to another medical conditions-**Medical conditions like hypothyroidism, heart disease, Parkinson's disease, and cancer can cause depression, which can improve if treated properly.[13]

- **Seasonal affective disorder-**This is a form of major depressive disorder that typically arises during the fall and winter and goes away during the spring and summer.[14]

- **Atypical depression-**Major depressive disorder with atypical features, characterized by temporary mood improvement in response to positive events, increased appetite, and rejection sensitivity, differs from typical depression.[15]

Data on depression per year (2021-2024)

S.no.	Year	Men	Women	Percentage
1.	2021	33%	35%	34%
2.	2022	37%	36%	36.5
3.	2023	25%	45%	35%

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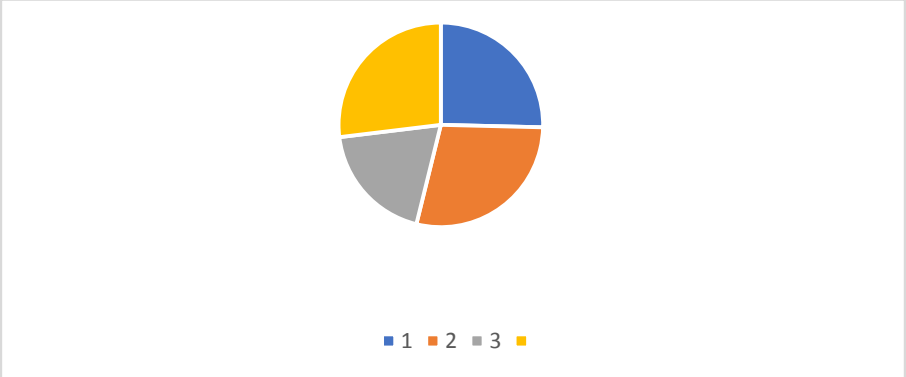
4.	2024	35%	47%	41%

Table.1 Data on Depression per year (2021-2024)[16,17,18]

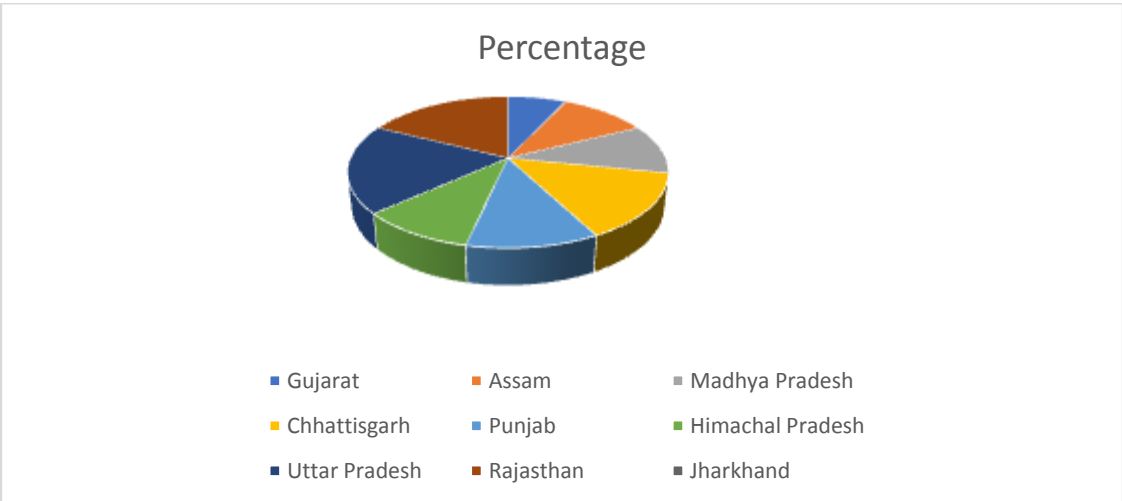


Pie chart representing Depression Year wise

Survey on Depression State wise

S.No.	State	Percentage(%)
1.	Gujarat	1.00%
2.	Assam	1.50%
3.	Madhya Pradesh	1.50%
4.	Chhattisgarh	2.00%
5.	Punjab	1.60%
6.	Himachal Pradesh	1.40%
7.	Uttar Pradesh	2.7%
8.	Rajasthan	2.51%
9.	Jharkhand	4.50%

Table.2 Data on depression case State wise[19,20,21,22]



Therapies used in depression-

1.Cognitive Therapy-

Cognitive behavioural therapy (CBT) is a psychological treatment that has been proven effective for various problems, including depression, anxiety disorders, alcohol and drug use issues, marital problems, eating disorders, and severe mental illness. CBT leads to significant

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improvement in functioning and quality of life, often being as effective or more effective than other forms of therapy or psychiatricmedications.[24]CBT is based on several core principles, including the idea that psychological problems are based on faulty or unhelpful thinking, learned patterns of unhelpful behaviour, and people can learn better ways of coping with them. Treatment typically involves efforts to change thinking patterns, such as recognizing distortions in thinking and reevaluating them in light of reality, understanding others' behaviour and motivation, using problem-solving skills, and developing confidence in one's abilities.[25]

Behavioural patterns are also addressed through strategies like facing fears, using role playing, and learning to calm one's mind and relax their body. The psychologist and patient/client work together collaboratively to develop an understanding of the problem and a treatment strategy. CBT therapists focus on helping individuals learn to be their own therapists, developing coping skills and changing their own thinking, emotionsandbehaviour. CBT therapists emphasize the person's current life rather than the history leading up to their difficulties, focusing on moving forward in time to develop more effective ways of coping with life.[26,27,28,29]

2.Interpersonal Therapy –

IPT is a 12- to 16-week treatment involving three phases: beginning, middle, and end. The therapist diagnoses major depression using DSM-IV or ICD-10 criteria and severity measures like the Hamilton Depression Rating Scale or Beck Depression Inventory. They also conduct an "interpersonal inventory" to review the patient's relationships, intimacy, and current relationships. The focus of treatment is on interpersonal deficits, which refer to the absence of a significant life event. In cases where a significant life event is absent, the focus is on interpersonal deficits, which are often confused with the absence of a current life event. The therapist uses these measures to reify the problem as an illness rather than a idiosyncratic defect.[35,36,37]

3.Vagus Nerve Stimulation Therapy –

Vagus nerve stimulation (VNS) is a promising treatment for various medical and neuropsychiatric disorders, with its potential to treat neurological and psychiatric disorders, inflammatory and immune disorders, pain-related disorders, cardiovascular diseases, and autonomic dysfunction. Historically, VNS was effective for epilepsy and major depression. Over the past few decades, VNS has gained approvals in obesity, post-stroke motor rehabilitation, and migraine. With increasing interest in VNS for various conditions, ongoing investigations are likely to lead to additional approvals.[30]The vagus nerve has numerous functions and innervates various end-organs throughout the chest and abdomen, highlighting its therapeutic potential for various conditions. However, access to VNS has been limited due to the invasive and expensive nature of implanted VNS.[31] The recent development of noninvasively forms of VNS has opened the door for scientists to study the effects of vagal stimulation more closely.Additionally, closed-loop VNS systems are beginning to make their way into research and clinical domains.In the era of personalized medicine, researchers are studying ways to make VNS treatments individualized and unique. There is still much to learn about this modality, and current gaps in the literature will be explored in the following sections.[32,33,34]

4. **Electro Convulsion Therapy –**

Severe depression leads to pathophysiologic changes in brain regions, including reduced activity and volumetric reductions in the frontal lobes, altered emotional stimuli processing in the ventral and orbital frontal cortex, and functional alterations in the hippocampus, Para hippocampal gyri, and amygdala.[38] The hypothalamic-pituitary-adrenal (HPA) axis becomes hypersensitive to stressors, exhibiting chronically elevated stress hormone levels and impaired feedback regulation. The Mes corticolimbic dopamine system and HPA axis are activated in patients with stress, affecting essential functions like concentration, motivation, and pleasure.[39,40,41]

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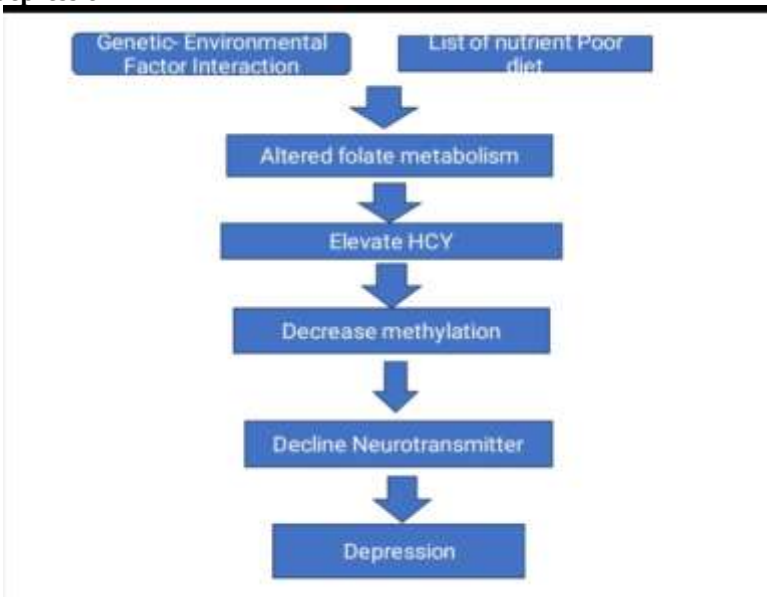
Pathophysiology of depression



Antidepressants:-Antidepressants are a medication used to treat clinical depression, OCD, generalized anxiety disorder, PTSD, and chronic pain, and can also be used to treat other conditions like obsessive-compulsive disorder, generalized anxiety disorder, and PTSD.[46,4]

Approvable Drugs (Antidepressants)

S.no.	Name of Drugs	Mechanism of action	Side effect	Adverse Effects	Metabolism
1.	Fluoxetine	It works by inhibiting the presynaptic reuptake of serotonin neuro transmitter.	• Headache • Nausea • Diarrhoea • Feeling Tired	• Anxiety • Heart burn • Dry mouth • Headache	It metabolizes in liver by CYPP-450. [48,49,50,51,52]
2.	Paroxetine	Itblocks the serotonin reuptake transporter which results in increase the conc. Of synaptic serotonin	• Head ache • Nausea • Dizziness • Fatigue	• Chest Pain • Edema • Tachycardia • Palpitation	It metabolize in liver by CYP-2D6. [53,54]
3.	Citalopram	It works by inhibition of CNS neuronal reuptake of serotonin	• Dry Mouth • Sweating • Headache • Nausea	• Nausea • Vomiting • Dizziness • Dry mouth	It metabolizes in liver by CYPP-450 and Mono Amino Oxidase [55,56]

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Non approvable Drugs (Anti-Depressants)

S.No.	Name of Drugs	Side Effect	Reason for Non-Approvable	
1.	Doxepin	• Bleeding gums • Chest tightness • Itching	Main Adverse effect is apnea and drowsiness so safe conditions was not established.	[57,58]
2.	Ketamine	• Redness • Pain • Irritation • Nausea	Ketamine has not been approved by FDA due to its low safety and low effectiveness.	[59,60]
3.	Trazodone	• Abnormal heartbeat • Skin infection	Heart rhythm and priapism are main Adr.	[61,62]

Mechanism of action of Anti-depressant

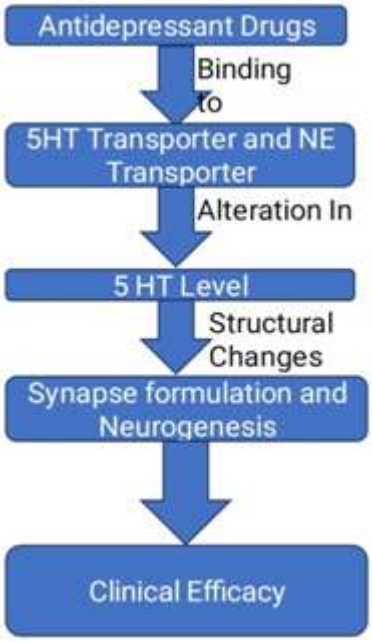

Fig.2 General mechanism of antidepressants[61,62,63,64]

Nutraceuticals used in treatment of depression

Nutraceuticals- Foods or parts of foods that are intended to have health benefits

Best Nutraceuticals used for treatment of Depression

The synthesis of neurotransmitters—brain chemicals that regulate mood and brain activity—requires vitamins. Vitamin deficiencies can affect dopamine and serotonin, which are involved in emotions of contentment and serenity. A lack of

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vitamins can also interfere with melatonin, which promotes sleep. Deficits in vitamins B, C, and D have also been associated with a higher risk of depression. Supplementing your diet and consuming foods high in these vitamins may help alleviate depressive symptoms naturally.

1. Vitamin B6 –

Serotonin, dopamine, and melatonin are neurotransmitters that require vitamin B6 to be produced. These brain chemicals give us feelings of pleasure, happiness, and calmness as well as facilitating sound sleep. The way that vitamin B6 functions is by assisting the body in breaking down the amino acids that comprise these chemicals. Insufficient intake of vitamin B6 impairs the synthesis of these neurotransmitters. Restoring vitamin B6 stores may help someone in recovery from depression because substance abuse frequently depletes them. Among the foods high in vitamin B3 are:

1.Animal proteins, including fish, poultry, and beef
2. Chickpeas and legumes
3. Nuts.

2. Vitamin B9-

Foods high in folate include spinach and other leafy greens, avocado, broccoli, whole grains, kidney beans, nuts, and seeds. Folate has been shown to reduce the symptoms of depression in people with low and normal levels of folate, and it also enhances the effectiveness of antidepressants. Vitamin B9, also known as folate, is involved in the production of serotonin, dopamine, and norepinephrine, neurotransmitters that help regulate mood and control the body's reaction to stress.

3. Vitamin C-

Vitamin C shields neurons from stress-induced damage and aids in signal transmission and reception in the brain. Any kind of disruption in brain transmission can lead to a number of problems, from dementia and schizophrenia to depression. Depression and exhaustion are typical symptoms of a vitamin C deficiency. Although vitamin C insufficiency is uncommon, research has indicated that taking supplements of the vitamin can elevate mood even in those who do not have a shortage.

4. Vitamin B12-

By lowering levels of the amino acid homocysteine, which can impair brain function, vitamin B12 influences mood and cognitive function. In addition to causing pernicious anaemia, a B12 deficiency has been linked to personality changes, sadness, and irritability.

5. Vitamin D-

Vitamin D is essential for the sleep-wake cycle and for controlling the metabolism of serotonin. The inability to fall or stay asleep due to a vitamin D deficit can negatively affect serotonin synthesis. Vitamin D deficiency is frequently observed in depressed individuals, and restoring storage might help alleviate symptoms.

Supplements For Depression-

For a healthy brain and mood, certain minerals, amino acids, and lipids are necessary. Depression symptoms may be exacerbated by deficiencies in tyrosine, magnesium, calcium, zinc, and omega-3 fatty acids. It has also been demonstrated that other supplements, including GABA, rhodiola rosea, SAMe, and St. John's wort, can help elevate mood, reduce anxiety, and increase the efficacy of antidepressants.

1. **Magnesium-**

Affects hundreds of bodily processes, including hormone and neurotransmitter functioning in the brain. It is believed to be particularly crucial for brain processes that lessen anxiety and stress. By controlling the stress response, magnesium helps reduce the symptoms of depression. Abuse of alcohol and other drugs can impair the body's absorption of magnesium, which frequently leads to low levels.

2. Calcium-

The activity of neurons, particularly those that regulate mood, is influenced by calcium. In addition to being necessary for the release of the neurotransmitters dopamine and serotonin into the brain, calcium may also have an impact on the neuronal tissues involved in emotional regulation. It has been demonstrated that raising calcium levels elevates mood.

3. Zinc-

Although zinc is necessary for numerous bodily functions, it is especially crucial for controlling how the brain reacts to stress. Depression, changed thinking, and a diminished capacity for learning can result from a zinc shortage. Supplementing with zinc can lessen the symptoms of depression and increase the efficiency of antidepressant drug.

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4. Omega- 3s-

One of the best-studied nutrients for improving mood is omega-3 fats. In the brain, omega-3 fatty acids interact with neurotransmitters. Because omega-3 fatty acids also have anti-inflammatory properties, they help prevent mood disorders including anxiety and despair. The structure of cells in the brain and nervous system is formed by DHA, a unique form of omega-3. Taking omega-3 supplements, particularly DHA, can greatly reduce depressive symptoms.

5 .St. John*s Wort-

For millennia, people have utilized the shrub known as St. John's wort for therapeutic purposes. It has been demonstrated that, when taken as a supplement, it can sometimes lessen the symptoms of mild depression just as well as prescription drugs. However, St. John's wort may not be safe to take with other medications because it interacts with a number of prescription pharmaceuticals, including SSRIs.

6. SAMe-

S-adenosyl-methionine, or SAMe, is a naturally occurring compound that can be found in a wide variety of plants and animals. Because it has a role in the synthesis of neurotransmitters and may enhance the effects of dopamine, it is frequently used as a supplement to treat depression. SAMe functions in tandem with vitamin B12 and folate, so taking all three supplements at once can help alleviate depression. It has also been demonstrated that SAMeincreases the efficacy of antidepressant drugs.

Taking SAMe instead of antidepressants has the advantage of being a natural solution for people who are unable to take drugs and having fewer negative effects. SAMe, however, can create serotonin syndrome and induce mania in bipolar illness patients when used with antidepressants. Always get your doctor's approval before taking SAMe.

7. Tyrosine-

The body produces the amino acid tyrosine, which is necessary for the synthesis of norepinephrine and adrenaline. Low tyrosine levels can result in depressive symptoms because tyrosine is also a precursor for dopamine. If dopamine production is compromised and levels are low, taking tyrosine may help reduce these symptoms.

8 .Rhodiola Rosea-

A root with adaptogenic qualities, rhodiola aids in the body's ability to handle stress and preserve equilibrium. Adaptogens control mood and energy by either stimulating or relaxing components of the stress response system. Taking rhodiola supplements may help reduce the symptoms of anxiety, despair, and exhaustion.

9. Amino Acids-

Some amino acids, like tyrosine, are needed to make neurotransmitters like serotonin and dopamine. The creation and balance of these brain chemicals can be affected by inadequate intake of certain amino acids, which can also exacerbate depressive symptoms. Popular amino acid supplements that are used to alleviate the symptoms of depression include tyrosine, 5-HTP, theanine, and tryptophan. They are beneficial because they have a direct role in the synthesis of neurotransmitters.

10 .GABA-

Gamma-aminobutyric acid, or GABA, is a neurotransmitter that encourages relaxation and serenity. GABA is in charge of lowering tension and may facilitate sound sleep. Because GABA and serotonin operate together, mood disorders and depressive symptoms may arise from low GABA levels.[65,66]

II. CONCLUSION-

Depression is a complex, multifaceted mental health condition that affects millions worldwide, influencing both emotional well-being and physical health. It can manifest in various forms, from mild to severe, and may involve symptoms like persistent sadness, fatigue, loss of interest, and disrupted sleep patterns. The condition is influenced by a combination of genetic, biological, environmental, and psychological factors, making it challenging to treat with a one-size-fits-all approach.

Antidepressants are one of the most commonly prescribed treatments for depression, primarily aimed at alleviating symptoms by adjusting the levels of neurotransmitters like serotonin, norepinephrine, and dopamine in the brain. These medications, which include classes such as SSRIs (Selective Serotonin Reuptake Inhibitors), SNRIs (Serotonin-Norepinephrine Reuptake Inhibitors), and others, have been shown to be effective for many individuals, particularly in moderate to severe cases of depression.

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However, antidepressants are not a cure-all. They can have side effects, and their effectiveness can vary from person to person. Some individuals may experience significant relief from symptoms, while others may find limited benefit or struggle with adverse reactions. It's also important to note that antidepressants typically take weeks to show noticeable effects and are most effective when combined with other forms of therapy, such as cognitive behavioural therapy (CBT), mindfulness, or lifestyle changes.

In addition, the decision to use antidepressants must be guided by a healthcare professional, who can monitor for potential side effects, drug interactions, and changes in symptoms. For some individuals, non-pharmacological interventions, like therapy, exercise, or lifestyle changes, might be more beneficial, or may be used alongside medication.

Ultimately, treating depression is a personalized journey, and antidepressants can be a valuable tool in the treatment plan for many people. However, they are most effective when part of a comprehensive approach that includes psychological support, lifestyle adjustments, and ongoing monitoring. The goal should always be to work toward long-term recovery and improved quality of life, while recognizing that depression is a condition that may require sustained attention and care. Ayurvedic, Homeopathic and some nutraceuticals and supplements are also used in treatment of depression such as ashwagandha, Brahmi, arsenic album, guduchi, vitamin B9 etc.

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