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Depression and Its Treatment: A Brief Review



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ABSTRACT

Depression has been the center stage in recent times due to the increase in suicidal rate and tendency among youth and in people due to various reasons that include personal reasons and stress in day to day life. People from all strata of society are facing the issue of depression but only a few are undergoing medical treatment. Depression is associated with mood changes or mood disorders. This disorder is characterized by intense and chronic feelings of sadness, grief, loss of interest in surroundings, or aggressiveness. It affects age groups like geriatric group, adolescents, post partum women and kids. It is one of the leading reasons for the increase in incidences of suicide amongst adolescent youth. The symptoms of depression vary according to the individual. Nowadays a range of treatments is available to treat depression which includes Antidepressant agents, Psychotherapy; Natural Herbs, and Miscellaneous therapies. Sometimes a combination of one or more of the treatments mentioned can be used to treat an individual having depression. This review gives a comprehension look in the treatment options available to an individual for depression.



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INTRODUCTION:

Depression is classified as mood disorder^[1] and is characterized by sadness, difficulty in thinking and concentration and an increase or decrease in appetite and abnormal sleep cycle. People who are depressed may feel dejected, hopeless and have a tendency to commit suicide^[2]. Globally around 264 million^[3] people are affected by depression which is a cause of concern. There are different types of depression and varied symptoms are observed in an individual according to their age groups and some predisposing factors.

Types:

Depression is classified depending upon the severity as Mild, Moderate and Severe^[4]. The major types of depression are: Major Depression and Persistent Depression.

a) Major Depression is the most severe form of depression. There are different subtypes of major depressive disorder, which include atypical features, anxious distress, mixed features, peripartum onset: during pregnancy or right after giving birth, seasonal patterns, melancholic features, psychotic features and catatonia. The person is said to be suffering from clinical depression when they are experiencing symptoms of depression for more than 5 years.

b) Persistent Depression: This type of depression is called as 'Dysthymia'^[5]. It is a milder form of depression and in order to be diagnosed with dysthymia, the person should experience the symptoms of depression for at least 2 years.

Symptoms:

The symptoms of depression vary from person to person and are also dependent upon a person's psychological, social and economic conditions. According to the different group of people, the symptoms are as follows:

a) **General symptoms**^[6]: These symptoms may be felt for more than 2 weeks:

- Feeling sad, anxious, or empty
- Feeling hopeless or pessimistic
- Feeling guilty, worthless, or helpless

- Loss of interest in surroundings
- Trouble with concentration, memory, or making decisions
- Abnormal sleeping time
- Appetite changes
- Gaining or losing weight
- Feeling restless or irritable
- Suicidal thoughts

b) Symptoms in adults^[7]: Depression occurs in older adults and is often undiagnosed and untreated. Many adults suffering from depression avoid seeking help when they're feeling down. The reason that depression in adults mostly goes untreated and undiagnosed is that the symptoms seen in these people are same like in other disorders or diseases. Examples of such symptoms are: fatigue, loss of appetite, sleep problems or loss of interest in sex. They may be not satisfied with life, bored, may feel helpless or worthless. They may want to stay at home and avoid social gatherings or socializing with people. Suicidal thinking or feelings in older adults is a sign of serious depression that should not go unnoticed. Of all people with depression, older adult men are at the highest risk of suicide.

c) Symptoms in Children and Teens: The risk and dangers of depression in children and teens is a matter of grave seriousness. Childhood trauma or any emotional trauma during early teens may cause depression in children and teens. This childhood depression may recur or may persist into their adulthood in the form of severe and grave illness^[8,9]. The symptoms are Refusal to go to school, clinging to parents or fear of losing a parent, loss of confidence, fear, refrains from playing with other children. Teenagers may show symptoms like constant sulking, easily irritable; feels misunderstood, and may include use of abusive substance, negative behavior and having disruptive or destructive thoughts. It is observed that girls in their teens are at more risk of having depression than boys^[10, 11].

d) Symptoms in Pregnancy: Pregnancy is duration in which the need to be aware about psychiatric changes in the women need to be looked after. These changes are mainly due to the changes in the hormones in the women's body required for the growth of foetus. It has

been seen that the occurrence of depression in pregnant women is similar to that in non pregnant women^[12, 13]. The symptoms include low self-esteem, hopelessness, poor concentration, and blunted affect, loss of interest and sleep or appetite disturbances^[14].

e) **Post partum depression**^[15]: It mainly is a combination of physical, emotional, hormonal and behavioral changes that occur in a woman after childbirth. Most of the first-time mothers may face “baby blues” after birth of child. The general symptoms that a postpartum woman can feel are as follows:

- Excessive tiredness and fatigue
- Changes in sleep pattern or abnormal sleep pattern
- Decreased libido
- Changes in appetite
- Frequent mood swings
- Sense of worthlessness, helplessness, and hopelessness



Factors or Causes^[16-19]:

There are many and varied factors that are responsible for depression. The exact cause of depression is unknown. Generally, depression results from a combination of recent or past events and other longer-term or personal factors. The factors are as follows:

1) Life Events:

- Long-term unemployment
- Living in an abusive or uncaring relationship
- Loneliness
- Stress at work
- Childhood physical or sexual abuse
- Financial difficulties

- Medical diagnosis (cancer, HIV, etc.),
- Bullying
- Loss of a loved one
- Social rejection, peer pressure, or bullying.

2) Personal Factors:

- Family history: Hereditary
- Personality: If a person has a tendency to be anxious or worries a lot, has low or no self esteem, needs to be a perfectionist, sensitive to criticism and has negative mindset.
- Chronic illness: People who are suffering from prolonged and chronic illness like cancer, HIV, Parkinson's disease or terminal end diseases are more susceptible to suffer from depression because of worry and fear.
- Drug and Alcohol Use: Prolonged use of Alcohol, Hallucinogens, Sedatives, Illicit drugs (Heroin, cocaine etc), Opioids and during withdrawal from the substance of abuse may result in depression.
- Medical Treatments: Some treatment regimens or therapies are responsible for inducing depression in the patient. Drug therapies include interferon therapy, beta-blockers, contraceptives, antipsychotics, hormonal agents; anticonvulsants are some therapies that may induce depression.

Treatments Available For Depression:

The treatment for depression can be classified as follows:

1. Medicinal Agents
2. Psychotherapy
3. Miscellaneous methods
4. Herbal drugs

1. Medicinal Agents^[20-33]:

These are the agents that help in elevating mood in the depressed person. The antidepressant agents mostly act on the monoaminergic pathways (MAO-A and MAO-B) by inhibiting uptake or reuptake of key neurotransmitters like serotonin (5-hydroxytryptamine), noradrenaline, adrenaline and dopamine. Based on this the antidepressant class of drugs were classified as RIMA (Reversible inhibitors of MAO-A), Tricyclic Antidepressants (TCA) which includes noradrenaline and 5-HT reuptake inhibitors and NA reuptake inhibitors; SSRI and Atypical antidepressants. The recent developments on understanding the neurobiology of depression novel pharmacologic and non-pharmacologic methods have been developed.

The Pharmacologic include: CRF (Corticotrophin releasing Factor) antagonists, Glucocorticoid receptor antagonist, Substance P antagonist, NMDA glutamate receptor antagonist, Transdermal selegiline, Dopamine D₃ receptor, Histone Deacetylase inhibitors, Neuropeptide Y antagonists, Melanocortin-4 receptor antagonists, GABA_B Receptor Modulators, GABA_A Receptor Modulator (Zuranolone), Glycogen synthase kinase 3 β inhibitors, SSRI with 5-HT_{1A}receptor partial agonist (Vilazodone), Relaxin-3 neuropeptide agonists or antagonist, triple uptake inhibitors (serotonin, noradrenaline and dopamine), erythropoietin pathway agents and increase in activity of typical antidepressants with atypical antidepressant agents.

The non-pharmacological methods of treating depression includes: brain stimulation techniques like electroconvulsive therapy (ECT), Transcranial direct current stimulation (tDCS), Repetitive transcranial magnetic stimulation (rTMS), Vagus nerve stimulation (VNS) and Light therapy. More clinical data is needed to evaluate the effectiveness, safety and efficacy of these methods.

2. Psychotherapy (Counselling)^[34-35]:

Sometimes treatment of depression does not require medication but can be treated by counselling done by certified psychologists or counsellors. This treatment takes longer to work. In some cases a combination of psychotherapy and antidepressants agents can be used to help a depressed person. It is of two types:

a) **Cognitive therapy:** It helps individuals to know the negative thoughts they have and learn to replace these thoughts with positive ones. This helps the individuals to get a more realistic picture and change their negative thought pattern.

b) **Interpersonal Therapy:** This therapy focuses on the role of relationships in a person's life and their communication with others. It helps a person learn how relationships might cause or maintain symptoms. The goal of this therapy is to reduce symptoms. More often the result of interpersonal therapy is that the individual experiences more satisfying relationships.

3. Miscellaneous methods:

The treatment of depression can be done by combining some unconventional methods with the standard treatment regimen. These methods usually take a long time to act depending upon the nature of the severity of depression and the willpower of an individual. Some of these methods are enlisted as:

- a) Meditation and Relaxation techniques
- b) Nutritional supplements and a balanced diet
- c) Omega-3 Fatty acid consumption
- d) Avoidance of alcohol and substance of abuse
- e) Daily Exercise
- f) Good and sound sleep
- g) Acupuncture
- h) Aromatherapy
- i) Bibliotherapy (Book reading)
- j) Yoga: A 8 week Hatha intervention in adults has shown satisfying results in treating mild to moderate depression.^[36]

4. Herbal Agents^[37-38]:

Plants of medicinal use have been the center of attraction for researchers working in the field of developing antidepressant agents because these plants have long been used to treat different diseases, including psychiatric disorders, and cause fewer adverse effects than synthetic and chemical drugs. Many patients find it difficult to tolerate the side effects of the synthetic or chemical drugs, do not respond adequately, and eventually lose their interest in continuing the drug regimen; other and major factor in individuals aversing from antidepressant or psychotherapy is the high costs making it difficult for the common man to go for allopathic or counseling treatment of depression, Currently, many herbal plants are under research and study to discover potential antidepressant effect. Some of the plants having antidepressant action are given in Table 1.

Table No. 1: Plants Showing Antidepressant Actions

| S. No | Plant Name | Family | Part Used | Extract Used |
|-------|--|----------------------------|-------------|----------------------------|
| 1 | <i>Anastatica hierochuntica L</i> [39] | Brassicaceae | Whole plant | Aqueous |
| 2 | <i>Abies webbiana</i> and <i>Berberis aristata</i> ^[40] | Pinaceae and Berberidaceae | Aerial part | Ethanollic |
| 3 | <i>Albizzia lebeck (Linn)</i> ^[41] | Mimosaceae | Bark | Ethanollic |
| 4 | <i>Amaranthus caudatus</i> ^[42] | Amaranthaceae | Whole plant | Methanollic |
| 5 | <i>Anacyclus pyrethrum</i> ^[43] | Compositae | Root | Hydroalcoholic |
| 6 | <i>Scutellaria baicalensis</i> ^[44] | Labiatae | Root | Methanollic |
| 7 | <i>Licium Chinese Mill</i> ^[45] | Solanaceae | Whole plant | Methanollic |
| 8 | <i>Artemisia capillaries Thunb</i> ^[46] | Asteraceae | Whole plant | Ethanollic |
| 9 | <i>Acorus tatarinowii Schott</i> ^[47] | Araceae | Rhizome | Essential oil |
| 10 | <i>Zizyphus xylopyrus (Retz.) Willd</i> ^[48] | Rhamnaceae | Whole plant | Ethanollic & Ethyl acetate |
| 11 | <i>Nelumbo nucifera</i> ^[49] | Nelumbonaceae | Leaves | |
| 12 | <i>Aronia melanocarpa Elliot</i> | Rosaceae | Fruits | Fruit Juice |

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|--------------|---|--------------------------|------------------|--|
| | [50] | | | |
| 13 | <i>Asperugo procumbens</i> L ^[51] | Boraginaceae | Aerial | Hydroalcoholic |
| 14 | <i>Angelicae dahuricae radix</i> ^[52] | Apiaceae | - | - |
| 15 | <i>Bacopa monnieri</i> ^[53, 54] | Scrophulariaceae | - | Ditilled water |
| 16 | <i>Boehmeria glomerulifera</i> Miq. ^[55] | Urticaceae | Leaves | Methanolic |
| 17 | <i>Brassica rapa subsp. Chinensis</i> ^[56] | Brassicaceae | Whole Plant | Methanolic |
| 18 | <i>Bupleurum yinchowense</i> ^[57] | Apiaceae | Dried roots | Ethanolic |
| 19 | <i>Butea monosperma</i> (Lam.) Kuntze ^[58] | Fabaceae | Stem | Methanolic |
| 20 | <i>Matricaria chamomilla</i> L ^[59] | Asteraceae | Flowers | Hydroalcoholic |
| 21 | <i>Cistanche deserticola</i> Y.M. Ca & <i>Cistanche tubulosa</i> ^[60] | Orobanchaceae | Herb | Decoction |
| 22 | <i>Citrus paradise</i> var. <i>Duncan</i> ^[61] | Rutaceae | Leaves | Petroleum ether, chloroform, methanol, and water |
| 23 | <i>Clitoria ternatea</i> L. ^[62] | Leguminosae (Fabaceae) | Leaves | Aqueous |
| 24 | <i>Couroupita guianensis</i> Aubl. ^[63] | Lecythidaceae | Root | Methanolic |
| 25 | <i>Cyperus rotundus</i> ^[64] | Cyperaceae | Rhizomes | 95% aqueous ethanol |
| 26 | <i>Echium vulgare</i> L. ^[65] | Boraginaceae | Aerial parts | Aqueous extract |
| 27 | <i>Eclipta alba</i> ^[66] | Asteraceae | Leaf | Ethanolic |
| 28 | <i>Trigonella foenum graecum</i> Linn. ^[67] | Fabaceae | Seeds | Methanolic |
| S. No | Plant Name | Family | Part Used | Extract Used |
| 29 | <i>Carthamus tinctorius</i> L. ^[68, 69] | Compositae or Asteraceae | Petals | Ethanolic and hydroethanolic |
| 30 | <i>Dacus carota</i> ^[70] | Apiaceae | Roots | Ethanol |

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|----|--|---------------|---------------------------|------------------------------------|
| | | | (Carrots) | |
| 31 | <i>Feijoa sellowiana</i> ^[71] | Myrtaceae | Fruit and leaf | Methanol |
| 32 | <i>Ficus platyphylla</i> Del ^[72] | Moraceae | Stem Bark | Methanol |
| 33 | <i>Ginkgo biloba</i> ^[73] | Ginkgoaceae | Green leaves | Ethanol |
| 34 | <i>Centella asiatica</i> ^[74] | - | - | Asiatic acid |
| 35 | <i>Hemerocallis citrina</i> ^[75] | Asphodelaceae | Flowers | Ethanol |
| 36 | <i>Hibiscus rosa sinensis</i> Linn. ^[76] | Malvaceae | Fresh flowers | Ethanol |
| 37 | <i>Hydrastis Canadensis</i> ^[77] | Ranunculaceae | Roots | Ethanol |
| 38 | <i>Hypericum perforatum</i> L ^[78,79,80] | Clusiaceae | Leaves and flowering tops | - |
| 39 | <i>Citrus Maxima</i> ^[81] | Rutaceae | Leaves | Aqueous |
| 40 | <i>Nardostachys jatamansi</i> ^[82,83] | Valerianaceae | Rhizomes | Ethanol |
| 41 | <i>Kielmeyera coriacea</i> ^[84] | Clusiaceae | Stems | Ethanol |
| 42 | <i>Emblica officinalis</i> ^[85] | Euphorbiaceae | Fruits | Aqueous |
| 43 | <i>Jatropha gossypifolia</i> ^[86] | Euphorbiaceae | Root | n-Hexane |
| 44 | <i>Kalanchoe Pinnata</i> (Lam) Pers ^[87] | Crassulaceae) | Stem | Aqueous and ethanolic |
| 45 | <i>Perillae Herba</i> ^[88] | Lamiaceae | - | Essential oil (l – perillaldehyde) |
| 46 | <i>Lavandula officinalis</i> ^[89] | Lamiaceae | Aerial parts | Hydroalcoholic |
| 47 | <i>Cymbogon citrates</i> ^[90] | Poaceae | Leaf | Aqueous |
| 48 | <i>Piper betle</i> Linn, <i>Piper cubeba</i> Linn. f., <i>Piper retrofractum</i> Vahl, <i>Piper longum</i> Linn. <i>Piper nigrum</i> Linn ^[91] | Piperaceae | Fruits | Ethanol |
| 49 | <i>Cajanus cajan</i> ^[92] | Leguminosae | Leaves | - |
| 50 | <i>Melissa officinalis</i> ^[93] | Lamiaceae | Leaves | Aqueous and Essential oil |
| 51 | <i>Mimosa pudica</i> ^[94] | Mimosaceae | Leaves | Aqueous |

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|----|---|---|-----------------------|---------------------------------|
| 52 | <i>Lagenaria siceraria</i> Standley (LS) syn. <i>L.</i> <i>leucantha</i> Rusby ^[95] | Cucurbitaceae | Fruits | Methanol |
| 53 | <i>Momordica cymbalaria</i> Hook. F. ^[96] | Cucurbitaceae | Fruits | Ethanollic |
| 54 | <i>Moringa oleifera</i> ^[97] | Moringaceae | Leaves | Ethanollic |
| 55 | <i>Morus alba</i> ^[98] | Moraceae | Root Bark | Methanollic |
| 56 | <i>Mucuna pruriens</i> ^[99] | Fabaceae | Seed | Distilled water |
| 57 | <i>Fumaria indica</i> Linn ^[100] | Fumariaceae | Whole plant | Ethanollic |
| 58 | <i>Ocimum basilicum</i> ^[101, 102] | Labiataeae | Whole plant, seeds | Methanollic, Petroleum ether |
| 59 | <i>Allium cepa</i> L. ^[103] | Amaryllidaceae | Bulb | Aqueous |
| 60 | <i>Origanum majorana</i> (L) ^[104] | Labiatae | Plant | Essential oil |
| 61 | <i>Panax ginseng</i> ^[105] | Araliaceae | Roots | - |
| 62 | <i>Passiflora incarnate</i> ^[106] | Passifloraceae | Flowers | Hydroalcoholic |
| 63 | <i>Passiflora foetida</i> ^[107] | Passifloraceae | Leaves | Methanollic |
| 64 | <i>Perilla frutescens</i> BRITTON var. <i>acuta</i> KUDO ^[108] | Labiatae | Leaves | - |
| 65 | <i>Pimpinella anisum</i> ^[109] | Umbelliferae | Fruit | Aqueous and Ethanollic |
| 66 | <i>Piper longum</i> ^[110] | Piperaceae | Fruit | Ethanollic |
| 67 | <i>Polygonum glabrum</i> Willd ^[111] | Polygonaceae | Leaves | Aqueous |
| 68 | <i>Portulaca oleracea</i> L. ^[112] | Portulacaceae, | Whole Plant | Aqueous |
| 69 | <i>Rosmarinus officinalis</i> L ^[113] | Labiatae | Stems and Leaves | - |
| 70 | <i>Schisandra chinensis</i> Baillon ^[114] | Schisandraceae | - | Aqueous |
| 71 | <i>Scutellaria</i> <i>baicalensis</i> , <i>Hericum</i> <i>erinaceus</i> and <i>Rhodiola rosea</i> ^[115] | Lamiaceae, Hericiaceae and Crassulaceae | - | - |
| 72 | <i>Hippophae rhamnoides</i> L. | Elaegnaceae | Fruits | Aqueous |

| | | | | |
|----|---|----------------|-----------------------|------------------------------------|
| | <i>Ssp. Turkestanica</i> ^[116] | | | |
| 73 | <i>Spirulina platensis</i> (Blue-green algae) ^[117] | Microcoleaceae | - | Dried powder |
| 74 | <i>Cynanchum auriculatum</i> Royle ex Wight ^[118] | Asclepiadaceae | Whole Plant | Ethanollic |
| 75 | <i>Uncaria lanosa Wallich var.</i> <i>appendiculata Ridsd</i> ^[119] | Rubiacea | Stems and hooks | Ethanollic |
| 76 | <i>Vigna Unguiculata</i> ssp. <i>Dekindtiana</i> (L.) Walp ^[120] | Fabaceae | Dried aerial parts | Aqueous |
| 77 | <i>Zea mays</i> ^[121] | Poaceae | Leaf | Ethanollic |
| 78 | <i>Crocus sativus L.</i> ^[122, 123] | Iridaceae | Stigma and petals | - |
| 79 | <i>Paeonia lactiflora</i> Pall ^[124] | Ranunculaceae | Root | Ethanollic |
| 80 | <i>Anemarrhena</i> <i>asphodeloides</i> BUNGE ^[125] | Liliaceae | Rhizome | - |
| 81 | <i>Glycyrrhiza glabra L</i> ^[126] | Fabaceae | - | Aqueous |
| 82 | <i>Bupleuri radix</i> ^[127, 128] | Apiaceae | - | Aqueous |
| 83 | <i>Cymbopogon</i> <i>martinii</i> (Roxb.) Wats. ^[129] | Poaceae | Leaves | Ethanollic |
| 84 | <i>Valeriana wallichii</i> DC ^[130] | Valerianaceae | Rhizome | Methanollic and Aqueous |
| 85 | <i>Bupleurum falcatum</i> ^[131] | Apiaceae | - | Methanollic |
| 86 | <i>Curcuma longa</i> ^[132] | Zingiberaceae | Rhizome | Aqueous |
| 87 | <i>Polygala tenuifolia</i> Willd., YZ ^[133] | Polygalaceae | Roots | Ethanollic |
| 88 | <i>Cynanchum</i> <i>auriculatum</i> Royle ex Wight ^[134] | Asclepiadaceae | - | - |
| 89 | <i>Hemerocallis citrina</i> Baroni ^[135, 136] | Asphodelaceae. | - | Phenolic extract and ethanollic |
| 90 | <i>Withania somnifera</i> ^[137] | Solanaceae | Roots | - |
| 91 | <i>Hibiscus sabdariffa</i> Linn. ^[138] | Malvaceae | Calyces | Etanolic |
| 92 | <i>Asparagus</i> | Liliaceae | Root | Hydroalcoholic |

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|-----|---|----------------|--------------|--|
| | <i>adscendens</i> Roxb. ^[139] | | | |
| 93 | <i>Sargassum fusiforme</i> ^[140] | Sargassaceae | - | Flucosterol |
| 94 | <i>Aloysia polystachya</i> (Griseb.) Moldenke ^[141] | Verbenaceae | Leaves | Hydroalcoholic |
| 95 | <i>Piper laetispicum</i> ^[142] | Piperaceae | - | Ethyl acetate |
| 96 | <i>Butea superba</i> ^[143] | Fabaceae | Roots | - |
| 97 | <i>Salvia elegans</i> Vahl ^[144] | Lamiaceae | Leaves | Hydroalcoholic |
| 98 | <i>Chrysactinia mexicana</i> A. Gray ^[145] | Asteraceae | - | Aqueous |
| 99 | <i>Terminalia catappa</i> ^[146] | Combretaceae | Leaf | Hydroalcoholic |
| 100 | <i>Schinus molle</i> L. ^[147] | Anacardiaceae | Aerial part | Ethanollic |
| 101 | <i>Nigella sativa</i> ^[148] | Ranunculaceae | Seed powder | Alcoholic |
| 102 | <i>Mitragyna speciosa</i> ^[149] | Rubiaceae | Leaves | - |
| 103 | <i>Allium macrostemon</i> ^[150] | Amaryllidaceae | - | Aqueous |
| 104 | <i>Trichilia catigua</i> ^[151] | Meliaceae | - | Hydroalcoholic |
| 105 | <i>Morinda officinalis</i> ^[152] | Rubiaceae | Roots | - |
| 106 | <i>Sonchus oleraceus</i> ^[153] | Asteraceae | Aerial parts | Hydroalcoholic and dichloromethanic |
| 107 | <i>Lafoensia pacari</i> A. St. Hil ^[154] | Lythraceae | - | Ethanollic |
| 108 | <i>Campis grandiflora</i> ^[155] | Bignoniaceae | Flowers | Ethyl acetate |
| 109 | <i>Asparagus racemosus</i> Linn. ^[156] | Asparagaceae | Roots | Methanollic |
| 110 | <i>Salvia sclarea</i> ^[157] | Lamiaceae | Leaves | Aromatic essential oil |
| 111 | <i>Marsilea minuta</i> Linn. ^[158] | Marsileaceae | - | Ethanollic |
| 112 | <i>Annona cherimolia</i> ^[159] | Annonaceae | Aerial Parts | Alkaloidal |

CONCLUSION:

Many recent research investigations are being carried out to elucidate the different mechanisms and pathways involved in the manifestation of depression. These research activities allow us to explore and research potential drug candidates that can help in the

treatment of depression. Natural products have more potential to act as antidepressant agents since they are multi constituent compounds and have lesser side effects and may act as an adaptogen. Polyherbal products are available that can help in elevating the mood. Many potential herbal products and plants are under investigation for their antidepressant action. The review highlights the different mechanisms, pathways, and proteins that may be involved in the manifestation of depression. These new findings pave the path for the discovery of more potent and efficacious anti-depressant agents with more specific action.

REFERENCES:

1. Depression; Last revised February 2018; <https://www.nimh.nih.gov/health/topics/depression/index.shtml>.
2. Depression (Mood); Last edited on 13 December 2020; [https://en.wikipedia.org/wiki/Depression_\(mood\)](https://en.wikipedia.org/wiki/Depression_(mood))
3. GBD 2017 Disease and Injury Incidence and Prevalence Collaborators. (2018). Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. *The Lancet*. DOI.
4. Depression; Key facts; 30 January 2020; <https://www.who.int/news-room/fact-sheets/detail/depression>
5. Everything you want to know about depression; Last reviewed on 3 December 2019; <https://www.healthline.com/health/depression>
6. Depression: Do you know the symptoms?; Reviewed by Jennifer Casarella on September 27, 2020; <https://www.webmd.com/depression/default.html>
7. Bhowmik D., Kumar K.P.S., Srivastava S, Paswan S, Dutta A.S. ; Depression - Symptoms, Causes, Medications And Therapies; *The Pharma Innovation*; Volume 1 No. 3; 2012; 37-51.
8. National Institute of Mental Health; U. S Department of Health and Human Services; National Institutes of Health NIH Publication No. 07-3561 Revised 2007
9. Weissman M M, Wolk S, Goldstein R B, Moreau D, Adams P, Greenwald Samaratne P et al; Depressed adolescents grown up; *Journal of the American Medical Association*, 1999; 281(18): 1701-1713.
10. Cyranowski JM, Frank E, Young E, Shear MK. Adolescent onset of the gender difference in lifetime rates of major depression. *Archives of General Psychiatry*, 2000; 57: 21-27.
11. Shaffer D, Gould MS, Fisher P, Trautman P, Moreau D, Kleinman M, Flory M. Psychiatric diagnosis in child and adolescent suicide. *Archives of General Psychiatry*, 1996; 53(4): 339-348.
12. Leslie Born, Dawn Zinga & Shauna Dae Phillips Update on the treatment of depression during pregnancy; *Therapy* (2006) 3(1), 153-161
13. O'Hara MW, Zekoski EM, Philipps LH, Wright E J; Controlled prospective study of postpartum mood disorders: comparison of childbearing and nonchildbearing women; *Journal of Abnormal Psychology*; 1990; 99(1), 3–15.
14. Felice E, Saliba J, Grech V, Cox J.; Prevalence rates and psychosocial characteristics associated with depression in pregnancy and postpartum in Maltese women; *Journal of Affective Disorders*; 82(2); 2004; 297–301.
15. Postpartum Depression; Reviewed by Michael W. Smith, MD on August 04 2020; <https://www.webmd.com/depression/guide/postpartum-depression#1>
16. [https://en.wikipedia.org/wiki/Depression_\(mood\)](https://en.wikipedia.org/wiki/Depression_(mood))
17. www.beyondblue.com
18. *Botts S, Ryan M.; Drug-Induced Psychiatric Diseases Chapter 18: Depression; Drug-Induced Diseases Section IV: pp. 1–23.*
19. *Arlington, VA; Diagnostic and statistical manual of mental disorders; fifth edition: American Psychiatric Association (2013).*
20. <http://www.blackdoginstitute.org.au/>
21. K.D. Tripathi; *Essentials of Medical Pharmacology; Sixth Edition; Jaypee Publishers; 439; 2003.*

22. Paul E. Holtzheimer III Charles B. Nemeroff; Advances in the Treatment of Depression; NeuroRX; Volume 3; Issue 1; January 2006; Pages 42-56.
23. Gian Marco Leggio, Salvatore Salomone, Claudio Bucolo, Vincenzo Micale, Filippo Caraci, Filippo Drago ; Dopamine D₃ receptor as a new pharmacological target for the treatment of depression; European Journal of Pharmacology; Volume 719; Issues 1–3; 5 November 2013, Pages 25-33.
24. Manabu Fuchikami, Shigeto Yamamoto, Shigeru Morinobu et al; The potential use of histone deacetylase inhibitors in the treatment of depression; Progress in Neuro-Psychopharmacology and Biological Psychiatry; Volume 64; 4 January 2016; Pages 320-324.
25. Andrew Holme, Markus Heilig, et al; Neuropeptide systems as novel therapeutic targets for depression and anxiety disorders; Trends in pharmacological sciences; Volume 24; Issue 11; November 2003; Pages 580-588.
26. Shigeyuki Chaki; Taketoshi Okubo; Melanocortin-4 Receptor Antagonists for the Treatment of Depression and Anxiety Disorders; Current Topics in Medicinal Chemistry, Volume 7; Number 11; 2007; pp. 1145-1151.
27. Daniela Felice Olivia F. O'Leary John F. Cryan; Targeting the GABA_B Receptor for the Treatment of Depression and Anxiety Disorders; GABA B Receptor; pp 219-250
28. Mehta, R., Bhandari, R., Kuhad, A., Kuhad, A.; Zuranolone. GABA-A receptor positive allosteric modulator, Treatment of major depressive disorder, Treatment of postpartum depression; Drugs Fut 2019, 44(6): 443.
29. J.F. Costemale-Lacost, J.P. Guilloux, R. Gaillard de L; The role of GSK-3 in treatment-resistant depression and links with the pharmacological effects of lithium and ketamine; Encéphale; Volume 42, Issue 2, April 2016, Pages 156-16.
30. Arif Khan; Vilazodone, a novel dual-acting serotonergic antidepressant for managing major depression; Expert Opinion on Investigational Drugs; Volume 18; Issue 11; 2009; Pages 1753-1764
31. Craig M. Smith, Andrew W. Walker, et al; Relaxin-3/RXFP3 networks: an emerging target for the treatment of depression and other neuropsychiatric diseases? Frontiers in Pharmacology; 21 March 2014.
32. Zhengming Chen & Phil Skolnick; Triple uptake inhibitors: therapeutic potential in depression and beyond; Expert Opinion on Investigational Drugs; Volume 16; Issue 9; 2007; pages 1365-1377.
33. Chongyang Ma, Fafeng Cheng et al; Erythropoietin Pathway: A Potential Target for the Treatment of Depression; International Journal of Molecular Sciences; 17; 2016; 677.
34. Anthony Cleare, CM Pariante and AH Young et al; Evidence-based guidelines for treating depressive disorders with antidepressants: A revision of the 2008 British Association for Psychopharmacology guidelines; Journal of Psychopharmacology; 2015, Vol. 29; (5); 459–525.
35. Non-Drug Approaches to Help Move from Depression to Feeling Happier with More Energy; created by David Rakel, 12 March 2017; https://www.fammed.wisc.edu/files/webfmuploads/documents/outreach/im/module_depression_patient.pdf
36. Sudha Prathikanti, Renee Rivera et al; Treating major depression with yoga: A prospective, randomized, controlled pilot Trial; PLoS ONE; 12(3); 2017; pgs 1-36.
37. Zahra Rabiei and Sana Rabiei; A Review on Antidepressant effect of medicinal plants; Bangladesh Journal of Pharmacology; 12; 2017; 1-11.
38. Yousuf Rather J, et al. Herbs as Antidepressants: A Review. Journal of Natural & Ayurvedic Medicine; 3(2); 2019.
39. Siham Abdoun, Tahani I. Hassan, Dalia A. Gaber, Amirah El- Sharekh; Antidepressant activity of *A. hierochuntica* L. effervescent granules using forced swimming test; Journal of Innovations in Pharmaceutical and Biological Sciences; Vol. 6 (2), Apr-Jun, 2019; 38-44.
40. Sucheta Gautam, Neetu Sachan, Alankar Shrivastav, Dilipkumar Pal; Evaluation of Antidepressant Activity of Ethanolic Extract of *Abies webbiana* and *Berberis aristata* in Laboratory Animals; Journal of Drug Delivery & Therapeutics; Volume 9 (1); 2019; 244-247.
41. Malarkodi Velraj, A. Vijayalakshmi, S. Jayakumari, S. Ramamoorthy. V. Ravichandiran & J. Srikanth; Antidepressant activity of the ethanolic extract of *Albizia lebeck* (Linn) bark in animal models of depression; Drug Invention Today; 1(2); 2009; 112-115.

42. B.S. Ashok Kumar, K. Lakshman, Saleemullakhan, C. Velmurugan, E.R. Vishwanath, S. Gopisetty; Evaluation of antidepressant like activity in *Amaranthus caudatus*; Mahidol University Journal of Pharmaceutical Sciences; 42 (1); 2015; 23-28.
43. S. R. Badhe, R. V. Badhe, M. M. Ghaisas, V. V. Chopade, A. D. Deshpande; Evaluations of antidepressant activity of *Anacyclus pyrethrum* root extract; International Journal of Green Pharmacy; April-June 2010; 79-82.
44. Weili Zhu, Shiping Ma, Rong Qu, Dali Kang & Yadong Liu; Antidepressant Effect of Baicalin Extracted from the Root of *Scutellaria baicalensis* in Mice and Rats; Pharmaceutical Biology; Vol. 44, No. 7, 2006, pp. 503–510.
45. Lee duk Ki, Gwak dong gul, Park sun dong; Antidepressant action of *Licium Chinese Mill* And its influence on indoleamine and its metabolites of depression model rats; The Korean Journal of Oriental Medical Prescription; volume 11 (2); 2003; pg. 185-196.
46. Soo-Hyun Park , Yun-Beom Sim , Pyung-Lim Han , Jin-Koo Lee & Hong-Won Suh; Antidepressant-like effect of chlorogenic acid isolated from *Artemisia capillaris* Thunb.; Animal Cells and Systems; Vol. 14, No. 4, December 2010, 253-259.
47. Ping Han, Ting Han, Wei Peng & Xiao-Ru Wang; Antidepressant-like effects of essential oil and asarone, a major essential oil component from the rhizome of *Acorus tatarinowii*; Pharmaceutical Biology; 51(5); 2013; 589–594.
48. Vimal Kant Sharma, Nagendra Singh Chauhan, Santram Lodhi, A.K. Singhai; Anti-Depressant Activity of *Zizyphus xylopyrus*; International Journal of Phytomedicine 1(2009); 12-17.
49. Min Gu Kang, Young Hwa Kim, A Rang Im, Byung Soo Nam, Sung wook Chae, Mi Young Lee; Antidepressant-like effects of *Nelumbo nucifera* leaves extract in chronic mild stress model; Korean Journal of Herbology; 29(2); 2014; 7-13.
50. Miroslav Eftimov, Stefka Valcheva-Kuzmanova; Antidepressant-Like Effect Of *Aronia Melanocarpa* Fruit Juice Applied Subchronically To Rats; Scripta Scientifica Medica, Vol. 45, Suppl. 6, 2013, Pp. 7-11.
51. Seyede-Atefeh Mirshafa, Mohammad Azadbakht and Nematollah Ahangar; Study of Antidepressant and Sedative-Hypnotic Activity of Hydroalcoholic Extract of *Asperugo procumbens* L. Aerial Parts in Mice; Iranian Journal of Pharmaceutical Research; 12 (3): (2013); 529-535.
52. Xiaosu Gu, Yong Zhou, Xiaomei Wu, Fen Wang, Cai-Yi Zhang, Chenchen Du et al; Antidepressant-like effects of auraptinol in mice; Scientific Reports; 4 : 4433.
53. Somoday Hazra, Ritabrata Banerjee, Biplab K. Das, Anup K. Ghosh, Tarit K. Banerjee, Uday S. Hazra, Susanta K. Biswas, Amal C. Mondal; Evaluation of Antidepressant activity of *Bacopa monnieri* in rat: A study in Animal Model of Depression; Drug discovery; 2(4); 2012; 8-13.
54. Sldv Ramana Murty Kadali, Das M.C, Srinivasa Rao A.S.R, Karuna Sri G; Antidepressant activity of Brahmi in Albino mice; Journal of Clinical and Diagnostic Research; Vol 8(3); March 2014; 35-37.
55. Muhammed M R, Sharmin KS, Md. Abdul Bari, Mohammad K I and Mohammad A. R; *Boehmeria glomerulifera* Miq. Exhibits *in vivo* Antidepressant and Antidiarrheal Activities; Bangladesh Pharmaceutical Journal; Volume 22(2); July 2019; 181-184.
56. Rahman MS, Jahan N, Rahman SMA, Rashid MA; Analgesic and antidepressant activities of *Brassica rapa* subspecies *chinensis* (L.) Hanelt on Swiss-albino mice model; Bangladesh Med Res Council Bulletin; 41; 2015; 114-120.
57. Xiuping Sun, Zhe Shi, Tengfei Li, Ruile Pan, Xinmin Liu, Lanlan Bu, Lingti Kong and Qi Chang; Antidepressant-like effects of total saikosaponins of *Bupleurum yinchowense* in mice; Journal of Medicinal Plants Research; Vol. 6(26), 11 July, 2012; pp.4308-4316.
58. Das Manas Kumar, Mazumder Papiya Mitra, Das Saumya, Das Sanjita; Antidepressant Potential Of Isolated Bioactive Compound From *Butea Monosperma* (Lam.) Kuntze; International Journal Of Social Sciences, 3(2), 225-236.
59. Jay D. Amsterdam, Qing S. Li, Sharon X. Xie, And Jun J. Mao; Putative Antidepressant Effect of Chamomile (*Matricaria Chamomilla* L.) Oral Extract in Subjects with Comorbid Generalized Anxiety Disorder and Depression; The Journal Of Alternative And Complementary Medicine; Volume 26, Number 9, 2020, Pp. 815–821.

60. Dongfang Wang, Haizhen Wang and Li Gu; The Antidepressant and Cognitive Improvement Activities of the Traditional Chinese Herb *Cistanche*; Hindawi Evidence-Based Complementary and Alternative Medicine; Volume 2017; Pgs. 1-9.
61. Vikas Gupta, Parveen Bansal, Pawan Kumar, Richa Shri; Anxiolytic And Antidepressant Activities Of Different Extracts From *Citrus Paradisi* Var. *Duncan*; Asian Journal Of Pharmaceutical And Clinical Research; Vol.3 Issue 2, April- June 2010; 98-100.
62. Arockiya Anita Margret, Violet Dhayabaran, Suvaiarasan Suvaitenamudhan and Subbiah Parthasarathy; Analysing the antidepressant and drug efflux competence of *Clitoria ternatea* L. as P-glycoprotein inhibitor to facilitate blood brain barrier; Acta Scientiarum. Biological Sciences; volume 41; 2019; pgs. 1-15.
63. Shaijesh S Wankhede, Manoj Gambhire, Archana Juvekar; *Couroupita Guianensis* Aubl: Evaluation Of Its Antidepressant Activity In Mice; Pharmacologyonline; 2; 2009; 999-1013.
64. Zhong-liu Zhou, Wen-Qing Yin, Ya-Mei Yang, Chun-Hong He, Xiao-Na Li, Cui-Ping Zhou and Hong Guo; New Iridoid Glycosides with Antidepressant Activity Isolated from *Cyperus rotundus*; Chemical and Pharmaceutical Bulletin; Volume 64 (1); 2016; 73-77.
65. Seyed Adel Moallem, Hossein Hosseinzadeh, Fatemeh Ghoncheh; Evaluation of Antidepressant Effects of Aerial Parts of *Echium vulgare* on Mice; Iranian Journal of Basic Medical Sciences; Vol. 10, No. 3, Autumn 2007, 189 – 196.
66. Mishra Swati, Jena Monalisa, Pal Abhisek; Evaluation of Antidepressant Activity Of *Eclipta alba* Using Animal Models; Asian Journal of Pharmaceutical and Clinical Research; Vol 6, Suppl 3, 2013, 118-120.
67. Vinod S.Pawar, Shivakumar Hugar, Bhagyashri Gawade and R.N.Patil; Evaluation of Antidepressant Like Activity of *Trigonella Foenum Graecum* Linn. Seeds in Mice; Pharmacologyonline 1; 2008;455-465.
68. Nasreen Qazi, Rafeeq Alam Khan and Ghazala H Rizwani; Evaluation of Antianxiety and Antidepressant Properties of *Carthamus Tinctorius* L. (Safflower) Petal Extract; Pakistan Journal Of Pharmaceutical Sciences; Vol.28, No.3, May 2015, Pp.991-995.
69. Saeid Abbasi-Maleki, Zahra Mousavi; Hydroethanolic extract of *Carthamus tinctorius* induces antidepressant-like effects: modulation by dopaminergic and serotonergic systems in tail suspension test in mice; Iranian Journal of Basic Medical Science; Vol. 20, No. 9, Sep 2017; 1063-1073.
70. Patibandla Naresh Babu, Nagaraju B, Yamini K, Dhananjanyulu M, Venkateswarlu K, Mubina M; Evaluation of Antidepressant Activity of Ethanolic Extract of *Dacus Carota* in Mice; Journal of Pharmaceutical Science & Research; Vol. 6(2), 2014, 73-77.
71. M. Mahmoudi, M.A. Ebrahimzadeh, M. Abdi, Y. Arimi, H. Fathi; Antidepressant Activities Of *Feijoa Sellowiana* Fruit; European Review For Medical And Pharmacological Sciences; 19; 2015; 2510-2513.
72. Shehu Aishatu, Ngbara Umami, Magaji Muhammad Garba, Yau Jamilu, Ahmed Abubakar; Antidepressant Activity of Methanol Stem Bark Extract of *Ficus platyphylla* Del (Moraceae) in Mice; Journal of Herbal Drugs; Vol. 8, No. 4; 2018; 227-234.
73. Hiroyuki Sakakibara, Kaori Ishida, Oliver Grundmann, Jun-Ichiro Nakajima, Shujiro Seo, Veronika Butterweck Et Al; Antidepressant Effect Of Extracts From *Ginkgo Biloba* Leaves In Behavioral Models; Biological and Pharmaceutical Bulletin; 29(8) ; 2016; 1767-1770 .
74. Tomas Eduardo Ceremuga, Debra Valdivieso, Catherine Kenner, Amy Lucia, Keith Lathrop, Owen Stailey, et al; Evaluation of the Anxiolytic and Antidepressant Effects of Asiatic Acid, a Compound from Gotu Kola or *Centella asiatica*, in the Male Sprague Dawley Rat; American Association of Nurse Anesthetists Journal; Vol. 83, No. 2 April 2015; 91-98.
75. Bingjian Du, Xiaoshuang Tang, Fei Liu, Chunyue Zhang, Guanghua Zhao, Fazheng Ren et al; Antidepressant-like effects of the hydroalcoholic extracts of *Hemerocallis Citrina* and its potential active components; BMC Complementary and Alternative Medicine 14 (326); 2014; 1-11.
76. Leena Khalid, Ghazala H Rizwani, Viqar Sultana, Hina Zahid, Raheela Khursheed and Huma Shareef; Antidepressant activity of ethanolic extract of *Hibiscus rosa sinensis* Linn.; Pakistan Journal of Pharmaceutical Science; Vol.27, No.5, September 2014, pp.1327-1331.
77. Sadia Batool, Haneen Saeed, Sarah Yehya, Rasha Ali, Afia Mofreh, Hanaa Saeed; Evaluation of Antidepressant Potential of *Hydrastis canadensis* in Mice; Macedonian Journal of Medical Sciences; 8(A); 2020 Aug 20; 589-592.

78. Md Sarfaraj Hussain, Md Zaheen Hasan Ansari, Muhammad Arif; Hyperforin: A lead for Antidepressants; International Journal of Health Research; 2(1); March 2009; 15-22.
79. Mario Wurglics & Manfred Schubert-Zsilavecz; *Hypericum Perforatum*: A 'Modern' Herbal Antidepressant; Clinical Pharmacokinetics; volume 45, 2006; pages 449–468.
80. S. S. Chatterjee, M. Nöldner, E. Koch, C. Erdelmeier; Antidepressant Activity of *Hypericum Perforatum* and Hyperforin: the Neglected Possibility; Pharmacopsychiatry 31; 1998; 7-15.
81. Vikram H. Potdar, Swati J. Kibile; Evaluation of Antidepressant-like Effect of *Citrus Maxima* Leaves in Animal Models of Depression; Iranian Journal of Basic Medical Sciences; Vol. 14, No. 5, Sep-Oct 2011, 478-483.
82. Dinesh Dhingra and Parveen Kumar Goyal; Inhibition of MAO and GABA: Probable antidepressants-like activity of *Nardostachys jatamansi* DC in mice; Indian Journal of Experimental Biology; volume 46; April 2008; 212-218.
83. Amritpal Singh, Anil Kumar, Sanjiv Duggal; *Nardostachys Jatamansi* Dc. Potential Herb With CNS Effects; Journal Of Pharmaceutical Research & Healthcare; Volume 1 (2); October 2009; 276-290.
84. Yara C.F. Goulart, Juliana V.C. Martins, Adair R. Santos, Leandro Y. Moreira, João Batista Calixto, Diógenes A.G. Cortez et al; Involvement of Serotonin in the Antidepressant like Effect of Extract from *Kielmeyera coriacea* Stems; Pharmaceutical Biology; 2007, Vol. 45, No. 3, pp. 169–175.
85. Dinesh Dhingra, Parul Joshi, Arun Gupta & Ritu Chhillar; Possible Involvement of Monoaminergic Neurotransmission in Antidepressant-like Activity of *Embllica officinalis* Fruits in Mice; CNS Neuroscience & Therapeutics; 18 (2012); 419–425.
86. Gabriel, B. O. And Idu, M.; Antidepressant And Anxiolytic Property Of *Jatropha Gossypifolia* N-Hexane Root Extract In Albino Mice; Sau Sci-Tech. Journal, 5(1), 2020.
87. Shashank Matthew, Ajay Kumar Jain, Cathrin Matthew, M.Kumar, Debjit Bhowmik; Antidepressant Activity Of Ethanolic Extract Of Plant *Kalanchoe Pinnata* (Lam) Pers In Mice; Indian Journal Of Research In Pharmacy And Biotechnology; Volume 1(2) March-April 2013; 153-155.
88. N. Ito, T. Nagai, T. Oikawa, H. Yamada and T. Hanawa; Antidepressant-like Effect of l -perillaldehyde in Stress-induced Depression-like Model Mice through Regulation of the Olfactory Nervous System; Evidence-Based Complementary and Alternative Medicine Volume 2011; 1-5.
89. Batoool Rahmati, Zahra Kiasalari, Mehrdad Roghani, Mohsen Khalili & Fariba Ansari; Antidepressant and anxiolytic activity of *Lavandula officinalis* aerial parts hydroalcoholic extract in scopolamine-treated rats; Pharmaceutical Biology, 2017; Vol. 55, No. 1, 958–965.
90. Dr.R.Mangaladevi; Evaluation of Antidepressant Effect of *Cymbopogon citratus* (Lemongrass) in Albino Mice; Dissertation Submitted for the Degree of M.D Branch–VI; Pharmacology April– 2017.
91. Mohib Khan; Comparative Physicochemical Evaluation of Fruits and Antidepressant Potential of Volatile Oils of Fruits of Local *Piper* Species; Oriental Journal of Chemistry; 2015, Vol. 31, No. (1); Pg. 541-545.
92. Yamin Liu, Ning Zhao, Chenchen Li, Qi Chang, Xinmin Liu, Yonghong Liao, Ruile Pan; Longistylone C acts antidepressant in vivo and neuroprotection in vitro against glutamate induced cytotoxicity by regulating NMDAR/NR2B-ERK pathway in PC12 cells; PLoS ONE 12(9); 2017; 1-19.
93. Emamghoreishi M., Talebianpour M.S.; Antidepressant effect of *Melissa officinalis* in the forced swimming test; DARU 2009 17 (1) 42-47.
94. Zoya Shaikh, Samaresh Pal Roy, Pankti Patel, Kashmira Gohil; Medicinal Value of *Mimosa Pudica* as an Anxiolytic and Antidepressant: A Comprehensive Review; World Journal of Pharmacy and Pharmaceutical Sciences; Volume 5, Issue 3, 420-432.
95. Rakesh Prajapati, Rahul Umbarkar, Sachin Parmar, Navin Sheth; Antidepressant like activity of *Lagenaria siceraria* (Molina) Standley fruits by evaluation of the forced swim behavior in rats; International Journal of Nutrition, Pharmacology, Neurological Diseases July 2011; Vol 1; Issue 2; 152-156.
96. Sai Vishal Daripelli, Vishwanath J, Vrushabendra Swamy Bm, Anil Kumar Reddy P; Antidepressant Activity Of Hydro-Alcoholic Extract Of Fruits Of *Momordica Cymbalaria* Hook. F In Animal Models; Journal of Chemical and Pharmaceutical Sciences; Volume 4 Issue 4; October – December 2011; 158-162.
97. Ginpreet Kaur, Mihir Invally, Resham Sanzagiri, Harpal S. Buttar; Evaluation of the antidepressant activity of *Moringa oleifera* alone and in combination with fluoxetine; Journal of Ayurveda & Integrative Medicine; October-December 2015; Vol 6; Issue 4; 273-279.

98. Dong Wook Lim, Jae-Woo Jung, Ji-Hae Park, Nam-In Baek, Yun Tai Kim In-Ho Kim, and Daeseok Han,; Antidepressant-like effects of sanggenon G, isolated from the root bark of *Morus alba*, in rats: involvement of the serotonergic system; *Biological and Pharmaceutical Bulletin*; August 2015; 1-19.
99. Dipanwita Pati, Dilip Kumar Pandey, Radhakrishnan Mahesh, Vadiraj Kurdekar, Hemant R. Jhadav; Antidepressant-Like Activity of *Mucuna Pruriens*: A Traditional Indian Herb in Rodent Models of Depression; *Pharmacologyonline* 1: 537-551 (2010).
100. Singh, G. K. And Kumar, V.; Neuropharmacological Screening and Lack Of antidepressant activity of Standardized Extract of *Fumaria Indica*: A Preclinical Study; *Journal of Pharmacology and Therapy* Vol. 3, 19-28 (2010); 19-28.
101. Basanti Brar, Joginder Singh Duhan, Pankaj Rakha; Antidepressant Activity Of Various Extracts From Seeds Of *Ocimum Basilicum* Linn.; *International Journal Of Scientific Research*; Volume : 4 Issue : 3; March 2015; 41-43.
102. Mehdi Abdoly, Alireza Farnam, Fatemeh Fathiazad, Arash Khaki, Amir Afshin Khaki, Arezoo Ibrahim, Fatemeh Afshari And Hossien Rastgar; Antidepressant-Like Activities Of *Ocimum Basilicum* (Sweet Basil) In The Forced Swimming Test Of Rats Exposed To Electromagnetic Field (Emf); *African Journal Of Pharmacy And Pharmacology* Vol. 6(3); 2012; Pp. 211-215.
103. Hiroyuki Sakakibara, Saki Yoshino, Yoshichika Kawai and Junji Terao; Antidepressant like effect of Onion (*Allium cepa* L.) powder in rat behavioural model of depression; *Bioscience, Biotechnology, Biochemistry*; 72; 2008; 70454-1-7.
104. Saeid Abbasi-Maleki, Zohre Kadkhoda, Rahim Taghizad-Farid; The antidepressant-like effects of *Origanum majorana* essential oil on mice through monoaminergic modulation using the forced swimming test; *Journal of Traditional and Complementary Medicine*; 10 (2020); 327-335.
105. Yang Jin, Ranji Cui, Lihong Zhao, Jie Fan, Bingjin Li; Mechanisms of *Panax ginseng* action as an antidepressant; *Cell Proliferation*; 52; 2009; 1-15.
106. Nima Jafarpoor, Saeid Abbasi-Maleki, Majid Asadi-Samani, Mir Hadi Khayatnouri; Evaluation of antidepressant-like effect of hydroalcoholic extract of *Passiflora incarnata* in animal models of depression in male mice; *Journal of HerbMed Pharmacology*; 3(1); 2014; 41-45.
107. Santosh P, Venugopl R, Nilakash A S, Kunjbihari S, Dr. Mangala L; Antidepressant Activity Of Methanolic Extract Of *Passiflora Foetida* Leaves In Mice; *International Journal Of Pharmacy And Pharmaceutical Sciences*; Vol 3, Issue 1, 2011; 112-115.
108. Takahiro Nakazawa, Takaaki Yasuda, Joji Ueda, And Keisuke Ohsawa; Antidepressant-Like Effects Of Apigenin And 2,4,5-Trimethoxycinnamic Acid From *Perilla Frutescens* In The Forced Swimming Test; *Biological And Pharmaceutical Bulletin*; 26(4); 2003; 474-480.
109. Zahra Shahamat, Saeid Abbasi-Maleki, Saeid Mohammadi Motamed; Evaluation of antidepressant-like effects of aqueous and ethanolic extracts of *Pimpinella anisum* fruit in mice; *Avicenna Journal of Phytomedicine*; 6 (3); 2006; 322-328.
110. Seon A Lee, Seong Su Hong, Xiang Hua Han, Ji Sang Hwang, Gab Jin Oh, Kyong Soon Lee Et Al; Piperine From The Fruits Of *Piper Longum* With Inhibitory Effect On Monoamine Oxidase And Antidepressant-Like Activity; *Chemical And Pharmaceutical Bulletin*; 53(7); 2005; 832—835.
111. Nizar, K., Sanghamitra Mishra., Tiwary, M.P., Singh, P.N. And Vikas Kumar; Antidepressant activity and Brain Neurotransmitters Study Of *Polygonum Glabrum Willd* In Rodents; *Journal Of Herbal Medicine & Toxicology*; 1(2); 2007; 73-79.
112. Soo-Jin Park, Min-Ji Choi, Sun-Yong Chung, Jong-Woo Kim, Seung-Hun Cho; The Involvement of AMPA Receptor in the Antidepressant-like Effects of the *Portulaca oleracea* L. Extract in Mice; *Journal of Oriental Neuropsychiatry* ; 24(3); 2013; 271-280.
113. D.G. Machado, V.B. Neis, G.O. Balen, A. Colla, M.P. Cunha, J.B. Dalmarco et al; Antidepressant-like effect of ursolic acid isolated from *Rosmarinus officinalis* L. In mice: Evidence for the involvement of the dopaminergic system; *Pharmacology, Biochemistry and Behavior*; 103; 2012; 204–211.
114. Min Gu Kang, Young Hwa Kim, A Rang Im, Byung Soo Nam, Sung Wook Chae and Mi Young Lee; Antidepressant-like Effects of *Schisandra chinensis Baillon* Water Extract on Animal Model Induced by Chronic Mild Stress; *Korean Journal of Medicinal Crop Science*; 22(3); 2014; 196 – 202.

- 115.Fiona Limanaqi, Francesca Biagioni, Carla Letizia Busceti, Maico Polzella, Cinzia Fabrizi and Francesco Fornai; Potential Antidepressant Effects of *Scutellaria baicalensis*, *Hericium erinaceus* and *Rhodiola rosea*; Antioxidants; 9 (234); 2020; 1-32.
- 116.Farhat Batool, Aisha Kamal, Madiha Sattar, Asad Hussain Shah, Syed Dilnawaz Ahmed, Zafar Saied Saify Et Al; Evaluation Of Antidepressant-Like Effects Of Aqueous Extract Of Sea Buckthorn (*Hippophae Rhamnoides* L. Ssp. *Turkestanica*) Fruits In Experimental Models Of Depression; Pakistan Journal Of Botany; 43(3); 2011; 1595-1599.
- 117.Suresh D, Madhu M, Saritha Ch, Raj Kumar V, Shankaraiah P; Antidepressant Activity Of *Spirulina Platensis* In Experimentally Induced Depression In Mice; International Journal Of Research And Development In Pharmacy And Life Sciences; Vol. 3, No.3; April-May 2014; Pp 1026-1035.
- 118.Cheng-Xue Ji, Xin-Ya Li, Shao-Bo Jia, Li-Li Liu, Yong-Chang Ge, Qing-Xiong Yang et al; The antidepressant effect of *Cynanchum auriculatum* in mice; Pharmaceutical Biology; 50(9); 2012; 1067–1072
- 119.Lieh-Ching Hsu, Yu-Jen Ko, Hao-Yuan Cheng, Ching-Wen Chang, Yu-Chin Lin, Ying-Hui Cheng et al; Antidepressant-Like Activity of the Ethanolic Extract from *Uncaria lanosa Wallich var. appendiculata Ridsd* in the Forced Swimming Test and in the Tail Suspension Test in Mice; Evidence-Based Complementary and Alternative Medicine; Volume 2012; 12 pages.
- 120.Akinpelu L. A, Adegbuyi T.A., Agboola S. S, Olaonipeku J. K, Olawuni I. J, Adegoke A. M et al; Antidepressant Activity and Mechanism of Aqueous Extract of *Vigna Unguiculata* ssp. *Dekindtiana* (L.) Walp Dried Aerial Part in Mice; International Journal of Neuroscience and Behavioral Science; 5(1); 2017;7-18.
- 121.Jude E. Okokon, Anwangabasi E. Udoh, Jackson Obot and Louis U. Amazu; Antidepressant activity of ethanol leaf extract of *Zea mays*; African Journal of Pharmacology and Therapeutics; vol.8 (1); 2019; pgs. 1-5.
- 122.Mojtaba Shafiee, Alireza Omranzadeh, Amirhossein Sahebkar; Saffron in the treatment of depression, anxiety and other mental disorders: Current evidence and potential mechanisms of action; Journal of Affective Disorders; Volume 227; February 2018, Pages 330-337.
- 123.Esmail Moshiri, Afshin Akhondzadeh Basti; Ahmad-Ali Noorbala; Amir- Hossein Jamshidi Seyed Hesameddin Abbasi Shahin Akhondzadeh; *Crocus sativus* L. (petal) in the treatment of mild-to-moderate depression: A double-blind, randomized and placebo-controlled trial; Phytomedicine; Volume 13, Issues 9–10; 24 November 2006, Pages 607-611.
- 124.Qing-Qiu, MaoSiu-Po, IpSam-Hip, Tsai Chun-Tao Che; Antidepressant-like effect of peony glycosides in mice; Journal of Ethnopharmacology; Volume 119, Issue 2, 26 September 2008, Pages 272-275
- 125.Li-Xiang Ren, Yi-Fan Luo, Xia Li, Dai-Ying Zuo, Ying-Liang Wu; Antidepressant-Like Effects of Sarsasapogenin from *Anemarrhena asphodeloides* BUNGE (Liliaceae); biological and Pharmaceutical Bulletin; volume 29(11);2006; Pages 2304-2306.
- 126.Dinesh Dhingra Amandeep Sharma; Antidepressant-like activity of *Glycyrrhiza glabra* L. in mouse models of immobility tests; Progress in Neuro-Psychopharmacology and Biological Psychiatry; Volume 30, Issue 3; May 2006; Pages 449-454.
- 127.Mi Kyoung Seo, Jae Chun Song, Sun Jung Lee, Kyung Ah Koo, Yong Ki Park, Jung Goo Lee et al; Antidepressant-like effects of *Bupleuri Radix* extract; European Journal of Integrative Medicine; Volume 4, Issue 4; December 2012; Pages 392-399.
- 128.Wu Dan ; Gao Yao ; Xiang Huan ; Xing Jie ; Han Yu Mei ; Qin Xue Mei ; Exploration into mechanism of antidepressant of *Bupleuri radix* based on network pharmacology; Acta Pharmaceutica Sinica; Vol.53 No.2; 2018; pp.210-219.
- 129.R. N. Gacche, R. U. Shaikh, S. M. Chapole, A. D. Jadhav & S. G. Jadhav; Kinetics of Inhibition of Monoamine Oxidase Using *Cymbopogon martinii* (Roxb.) WATS. A Potential Antidepressant Herbal Ingredient with Antioxidant Activity; Indian Journal of Clinical Biochemistry; volume 26; 2011; pages 303–308.
- 130.Fazal Subhan, Nasir Karim, Anwarul Hassan, Gilani Robert, D. E. Sewell; Terpenoid content of *Valeriana wallichii* extracts and antidepressant-like response profiles; Phytotherapy Research; Volume 24, Issue 5; May 2010; Pages 686-691.
- 131.Sunoh Kwon, Bombi Lee, Myunghwan Kim, Hyejung Lee, Hi-Joon Park, Dae-Hyun Hahm; Antidepressant-like effect of the methanolic extract from *Bupleurum falcatum* in the tail suspension test; Progress in Neuro-Psychopharmacology and Biological Psychiatry; Volume 34, Issue 2; 17 March 2010; Pages 265-270

- 132.Kulkarni S.K., Akula K.K., Deshpande J.; Evaluation of Antidepressant-Like Activity of Novel Water-Soluble Curcumin Formulations and St. John's Wort in Behavioral Paradigms of Despair; *Pharmacology*; 89; 2012; 83-90.
- 133.P.Liu, Y. Hu, D.-H.Guo, D.-X.Wang, H.-H.Tu, L.Ma et al; Potential antidepressant properties of Radix Polygalae (Yuan Zhi); *Phytomedicine*; Volume 17, Issue 10, August 2010, Pages 794-799.
- 134.Qing-XiongYang, Yong-ChangGe, Xiao-YanHuang, Qian-YunSun; Cynanauriculoside C–E, three new antidepressant pregnane glycosides from *Cynanchum auriculatum*; *Phytochemistry Letters*; Volume 4, Issue 2; 15 June 2011; Pages 170-175.
- 135.PanXu, Ke ZhuWang, CongLu, Li MingDong, JunLe Zhai Yong, HongLiao et al; Antidepressant-like effects and cognitive enhancement of the total phenols extract of *Hemerocallis citrina* Baroni in chronic unpredictable mild stress rats and its related mechanism; *Ethnopharmacology*; Volume 194; 24 December 2016; Pages 819-826.
- 136.LanGu, Yan-JunLiu, Yao-Bin, WangLi-TaoYi; Role for monoaminergic systems in the antidepressant-like effect of ethanol extracts from *Hemerocallis citrina*; *Journal of Ethnopharmacology*; Volume 139, Issue 3; 15 February 2012; Pages 780-787.
- 137.S.K.Bhattacharya, A.Bhattacharya, K.Sairam, S.Ghosal; Anxiolytic-antidepressant activity of *Withania somnifera* glycowithanolides: an experimental study; *Phytomedicine*; Volume 7, Issue 6; December 2000; Pages 463-469.
- 138.Gulsheen, Ashwani Kumar & Anupam Sharma; Antianxiety and Antidepressant Activity Guided Isolation and Characterization of Gossypetin from *Hibiscus sabdariffa* Linn. Calyces; *Journal of Biologically Active Products from Nature* Volume 9, Issue 3; 2009; Pages 205-214.
- 139.Priyanka Pahwa and Rajesh Kumar Goel; Antidepressant-like effect of a standardized hydroethanolic extract of *Asparagus adscendens* in mice; *Indian Journal of Pharmacology*; 51(2); Mar-Apr 2019; 98–108.
- 140.Xing-Hua Zhen, Ying-Chun Quan, Hai-Ying Jiang, Zheng-ShunWen, You-Le Qu; Fucosterol, a sterol extracted from *Sargassum fusiforme*, shows antidepressant and anticonvulsant effects; *European Journal of Pharmacology*; Volume 768; 5 December 2015; Pages 131-138
- 141.S. Mora, G. Díaz-Véliz, R.Millán, H.Lungenstrass, S. Quirós, T. Coto-Morales et al; Anxiolytic and antidepressant-like effects of the hydroalcoholic extract from *Aloysia polystachya* in rats; *Pharmacology Biochemistry and Behavior*; Volume 82, Issue 2, October 2005, Pages 373-378.
- 142.Hui Xie, Ma-chengYan, Di Jin, Jia-jia Liu, MinYu, Dong Dong; Studies on antidepressant and antinociceptive effects of ethyl acetate extract from *Piper laetispicum* and structure–activity relationship of its amide alkaloids; *Fitoterapia*; Volume 82, Issue 7; October 2011; Pages 1086-1092.
- 143.Daishu Mizuki, Kinzo Matsumoto, Ken Tanaka, Xoan Thi Le, Hironori Fujiwara, Tsutomu Ishikawa; Antidepressant-like effect of *Butea superba* in mice exposed to chronic mild stress and its possible mechanism of action; *Journal of Ethnopharmacology*; Volume 156, 28 October 2014, Pages 16-25.
- 144.S.Mora, R.Millán, H.Lungenstrass, G.Díaz-Véliz, J.A.Morán, M.Herrera-Ruiz; The hydroalcoholic extract of *Salvia elegans* induces anxiolytic- and antidepressant-like effects in rats; *Journal of Ethnopharmacology*; Volume 106, Issue 1; 15 June 2006, Pages 76-81.
- 145.Cassani J, Octavio A, Ferreyra-Cruz, Ana María, Dorantes-Barrón, Rosa María; Antidepressant-like and toxicological effects of a standardized aqueous extract of *Chrysactinia mexicana* A. Gray (Asteraceae) in mice; *Journal of Ethnopharmacology* Volume 171; 2 August 2015; Pages 295-306.
- 146.Y.Chandrasekhar, E.M. Ramya, K.Navya, G.Phani Kumar, K.R.Anilakumar; Antidepressant like effects of hydrolysable tannins of *Terminalia catappa* leaf extract via modulation of hippocampal plasticity and regulation of monoamine neurotransmitters subjected to chronic mild stress (CMS); *Biomedicine & Pharmacotherapy*; Volume 86; February 2017; Pages 414-425.
- 147.Machado D. G, Bettio L.E.B, Cunha M. P, Santos A.R. S, Pizzolatti M. G, Inês M. C. Brighente; Antidepressant-like effect of rutin isolated from the ethanolic extract from *Schinus molle* L. in mice: Evidence for the involvement of the serotonergic and noradrenergic systems; *European Journal of Pharmacology* Volume 587, Issues 1–3, 10 June 2008, Pages 163-168.
- 148.Ahirwar Dheerajand Ahirwar Bharti; Antidepressant effect of *Nigella sativa* in stress-induced depression; *Research Journal of Pharmacy and Technology* Year: 2020, Volume: 13, Issue: 4; pgs.1611-1614.

- 149.N.Farah Idayu, M. Taufik Hidayat, M. A. M .Moklas, F. Sharida, A .R. Nurul Raudzah et al; Antidepressant-like effect of mitragynine isolated from *Mitragyna speciosa* Korth in mice model of depression; Phytomedicine; Volume 18, Issue 5; 15 March 2011; Pages 402-407.
- 150.Seungjoo Lee, Dong Hyun Kim, Chang Hwan Lee, Ji Wook Jung, Yong Taek Seo, Young Pyo Jang; Antidepressant-like activity of the aqueous extract of *Allium macrostemon* in mice; Journal of Ethnopharmacology; Volume 131, Issue 2; 15 September 2010; Pages 386-395
- 151.Campos M. M, Fernandes E. S, Ferreira J, Adair R. S. Santos & João B. Calixto; Antidepressant-like effects of *Trichilia catigua* (*Catuaba*) extract: evidence for dopaminergic-mediated mechanisms; Psychopharmacology; volume 182; 2005; pages45–53.
- 152.<https://europepmc.org/article/med/7626209>
- 153.Fabiana Cardoso, Vilela Marina de Mesquita, Padilha Geraldo, Alves-Da-Silva, Roseli Soncini and Alexandre Giusti-Paiva; Antidepressant-Like Activity of *Sonchus oleraceus* in Mouse Models of Immobility Tests; Journal of Medicinal Food; Vol.. 13(1).
- 154.P.M.Galdino, M.V.M.Nascimento,B.L.Sampaio, R.N.Ferreir, J.R.Paula, E.A.Costa; Antidepressant-like effect of *Lafoensia pacari* A. St.-Hil. ethanolic extract and fractions in mice; Journal of Ethnopharmacology; Volume 124, Issue 3; 30 July 2009; Pages 581-585.
- 155.Hai- Chuan Yu, Jiao Wu, Hong- Xing Zhang, Hai- San Zhang, Ting- Ting Qiao, Ji- Xia Zhang et al; Antidepressant- like and anti- oxidative efficacy of *Campsis grandiflora* flower; Journal of Pharmacy & Pharmacology; Volume 67, Issue 12;December 2015; Pages 1705-1715
- 156.Singh G.K, Garabadu D,Muruganandam A. V,Joshi V. K, Krishnamurthy S; Antidepressant activity of *Asparagus racemosus* in rodent models; Pharmacology Biochemistry and Behavior; Volume 91, Issue 3; January 2009; Pages 283-290.
- 157.Geun Hee Seol, Hyun Soo Shim, Pill-Joo Kim, Hea Kyung Moon, Ki Ho Lee, Insop Shim; Antidepressant-like effect of *Salvia sclarea* is explained by modulation of dopamine activities in rats; Journal of Ethnopharmacology; Volume 130, Issue 1; 6 July 2010; Pages 187-190.
- 158.Bhattamisra S. K, Khanna V.K, Agrawal A. K, Singh P. N, Singh S.K; Antidepressant activity of standardised extract of *Marsilea minuta* Linn.;Journal of Ethnopharmacology Volume 117, Issue 1; 17 April 2008; Pages 51-57.
- 159.M. Martínez-Vázquez, R.Estrada-Reyes, A.G.Araujo Escalona, I.Ledesma Velázquez, L.Martínez-Mota, J.Moreno,et al; Antidepressant-like effects of an alkaloid extract of the aerial parts of *Annona cherimolia* in mice; Journal of Ethnopharmacology; Volume 139, Issue 1; 6 January 2012; Pages 164-170.