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A COMPREHENSIVE REVIEW ON EXTENDED RELEASE TABLETS WITH ASHWAGANDHA AND VELVET BEAN FOR DEPRESSION

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ABSTRACTS

Depression is a psychological disorder that is characterized by depressed mood or loss of interest in activities, causing significant impairment in daily life. More than millions of people suffer from depression in all ages. There are different types of antidepressant drugs used to treat depression. About 80 % of world population trust on traditional herbal medicine for the primary health care. Now a days, herbal remedies are considered as dietary supplement for disease prevention as well as alternative medicine. In the world a wide varities of herbal medicine are available in the market. There are many herbal plants which are responsible for antistress activity. The study mainly focus on the combination effect of *Withania somnifera* and *Mucuna pruriens* for antidepressant activity. Based on literature review, The sitoindosides VII-X and Withaferin-A present in the Ashwagandha showing Antistress activity, have been shown to have significant anti-stress activity against acute models of experimental stress and also levodopa which is present in the velvet bean showing Antistress, neuroprotective as well as Antioxidant properties. The extended release dosageforms are important tool in medicinal practice and also offers a wide range of advantages to the patients. It is the most preferred route because of ease of administration. Extended release dosage form are those which release drug slowly, so that the plasma concentrations are maintained at a therapeutic level for a prolong period of time usually between 8-12hrs. It allows a reduction in dosing frequency and provide long action of the drug.

KEYWORDS: Depression, *Withania somnifera*, *Mucuna pruriens*, Extended release tablets.

INTRODUCTION

Depression is a mental illness characterized by pathological changes in mood and that will affect a person's thoughts, behavior, motivation, feelings, and sense of well-being. More than millions of people suffer from depression in all ages. Depression is the main disability and also it is the contributor to all diseases.[1] It is affected to women more than men and it also leads to suicide. It is entirely different from other mood disorders. The depression may be severe or serious, when the symptoms are lasting for longer period with moderate or severe intensity. It may first occure at any time, during the late teens to mid-20s.about 80% of people with depression are eventually respond to treatment. It is one of the treatable mental disorder.

Signs and Symptoms of depression

Common symptoms of depression include

Figure 1: Symptoms of depression.

- Feelings of sadness, hopelessness, worthlessness, or emptiness. Most of the time feeling down.
- Reduced interest in activities once enjoyed. This is because of lack of motivation and feel disinterested.
- Trouble sleeping or oversleeping. Sleeping too much or too little.
- Appetite or weight changes. Here the people may be over eating or lose appetiteand also experience unintentional weight gain or loss without dieting.

- Fatigue or decreased energy. People feels exhausted all the time.
- Difficulty thinking clearly or quickly, remembering details, concentrating, or making decisions. The people may experience difficulty in thinking, concentrating and they may fail to take decisions.
- Irritability, frustration, or pessimism, mood & headspace feel negative most of the time.
- Physical aches and pains. The people may have headaches or stomachache that cannot be treated with medication.
- Recurrent thoughts of death or suicide without a plan to actually do it.

Causes of depression

The depression is caused by not by a single cause but it occur by the combination of genetic, biological, environmental, and psychological factors

1. **Genetic factors**
2. **Psychological factors**
3. **Physical factors**
4. **Environmental factors**
5. **Biochemical factors**
6. **Other factors**

1. Genetic factors

Depression may be occur generation after generation in some families, but it can occur in people who have no family history of depression.[2] The researchers are determine that depressive illnesses can be inherited to some extends. This means that if someone have close relatives who have clinical depression, they may inherit a tendency to develop the illness. It does not mean that they are destined to become depressed. Bipolar disorder has a strong genetic influence. If any person with bipolar disorder, approximately 50% of their parent have a history of clinical depression. When a mother or father has bipolar disorder, their child will have a 25% chance of developing clinical depression. If both parents have bipolar disorder, the chance of their child also developing bipolar disorder is between 50% and 75%.

2. Psychological factors

People who are pessimists, who have self-esteem, or who are readily overwhelmed by stress are prone to depression. Whether this represents a psychological predisposition or an early form of the illness is not clear.

3. Physical factors

Many medical illness such as stroke, heart attack, cancer, endocrine disorders like diabetes, hypothyroidism can result in depressive episodes in some people.

4. Environmental and Social factors

Environmental causes of depression include events such as stress, traumatic events and childhood difficulties, synthetic chemicals, noise pollution &Natural and Catastrophic Disasters.

Stress: The reaction of the individual's mind and body to stress, and the development of clinical depression there were showing very complex relationship. In case of some people there is a direct relationship between a stressful event and the development of depression. The stress can be negative or positive. Thenegative stress are loss of a loved one, loss of a job, loss of a relationship and divorce. The positive stress are planning for a wedding, preparing for a new job, and moving to a new city. The negative and positive stress from the environmental event will causes depression.

Childhood difficulties: Most of the studied shows that higher rates of clinical depression were occur in people with severe difficulties in childhood. Sexual, emotional, or physical abuse, upbringing, parental separation, and mental illness in one or both of the parents these are the major childhood difficulties. The separation or death of a parent before the age of eleven is the most difficult emotional event for child. Childrens that they have experienced this type of emotional event also shows a higher chances of developing depression.

Traumatic events: In case of some people have experienced a traumatic event before developing depression. loss of a loved one, a serious medical illness, the end of a marriage or significant financial loss these are some of traumatic event. These types of events can destroy the sense of control and stability in a person's life and that may lead to leading to emotional distress.

Synthetic chemicals: In our everyday life we are consuming different type of synthetic chemicals from preservatives, additives and hormones that are found and added to so many of our foods, pesticides that are sprayed. Now a days the Synthetic chemicals and pollutants are act as a link to depression and Major Depressive episodes.

Noise pollution: Studies are shows that the continual exposure to noise pollution cardiovascular diseases and increased blood pressure, aggression increased stress levels, hearing loss and disruptions in sleep that are linked to severe depression, panic attacks and forgetfulness.

Natural and Catastrophic disasters: Hurricanes, earthquakes, or fires, and even manmade disasters such as bombings and war these will pushes an already good conditional person into a severe Major Depression.

5. Biochemical factors

The human knowledge about the brain is still limited, so that do not really know what actually happens in the brain to cause depression. But the hypothesis by different researchers are suggest that in most of the case of clinical depression, neurotransmitter function is disrupted. Neurotransmitters are chemicals that carry signals from one part of the brain to the another part of the brain. serotonin, noradrenaline and dopamine are the main three neurotransmitters that affect a persons mood . In normal brain function, neurotransmitters interact with a series of nerve cells, signal being transmitted. But, in people with depression, neurotransmitters fail to function normally for regulating mood, so that the signal transmission doesn't occur, that will lead to depression.

6. Other factors

There are many other factors that will causes depression that are,

Personality – The research studies shows that people with the following personality types are on high risk for developing clinical depression than the others.

1. People with High levels of anxiety, which can be experienced as an internalised 'anxious worrying' style.
2. people with more Shyness they may tend to become avoiding the social contact or they may become reserve personally.
3. Self-criticism or low self-worth.
4. The people with more Perfectionism causes the depression.

Drug and Alcohol use – Drug and aicohol use both lead to depression. Many of the people with depression have a history of certain drug and alcohol use. Thelong term use of certain medications such as sleeping aids and blood pressure medication that may also cause symptoms of depression**.**

Gender- Gender is an another factor. Studies are shows that in women the chances of developing non-melancholic depression is higher than men. Internalised stress, unsatisfactory marriage, hormonal changes these are some of the explanations for women are experiencing depression than men.

Types of depression

Major depressive disorder(MDD)

It is the most common type of depression. It is also called as unipolar depression or clinical depression. Reduced interest in activities once enjoyed, depressed mood, Fatigue or decreased energy, Appetite or weight changes, difficulty in thinking and in concentration, recurrent thoughts of death and suicide these are the key features of Major depressive disorder.[3]

Persistent Depressive Disorder (PDD)

Persistent Depressive Disorder is also called as Dysthymia. It is a type of chronic depression. It may last for more than at least 2 year. It can be mild, moderate, or severe. People withpersistent depressive disorder might experience short periods of not feeling depressed, but the symptoms lasts for at least two months. This type of depression is long lasting but the symptoms are not severe. Loss of interest and pleasure, Anger and irritability, Feelings of guilt, Feelings of sadness, Low self-esteem & Sleeping too much these are some of symptoms of Persistent Depressive disorder.

Bipolar disorder

Bipolar disorder is also called as manic depression. The person experiences periods of depression and mania with periods of normal mood in between them. Mania is a period of abnormally elevated mood. The symptoms of mania is highly differ from the symptoms of depression. Person feeling great, having plenty of energy, racing thought, little need of sleep and talking fast these are some of the symptoms of mania. The person with bipolar disorder they loses touch with reality and experience especially about their ideas and abilities and they also experiences hallucinations. Treatment of bipolar disorder is entirely differ from depression.

Postpartum depression

After delivery, because of the hormonal shifts many women experience postpartum Depression. It is called as “baby blues.” feelings of sadness, Mood changes, Trouble bonding

with your baby, recurrent thoughts of suicide and hurting yourself or your baby, anxiety, irritability these are some of the symptoms of depression. The symptoms are severe and longer-lasting. The condition may last up to a year if untreated.

Premenstrual Dysphoric Disorder (PMDD)

It is a type of depression that occurs during the second half of the menstrual cycle**.** Fatigue, Feeling sad, hopeless and helplessness, feelings of stress or anxiety, Mood swings, Irritability, Difficulty to concentrate and Food cravings these are some of the symptoms of Premenstrual Dysphoric Disorder.

Seasonal Affective Disorder (SAD)

Seasonal Affective Disorder is a specific type of depression which is occurring in a seasonal pattern. In winter season some people experience depression, sleepiness and weight gain then the condition is called as seasonal affective disorder. But at the same time those people feel perfectly fine in the spring season.

The SAD may be caused due to the variation in light exposure in different season. Loss of energy, sleep too much and weight gain these are some of symptoms. These may be last up to 2 to 3 years.

Atypical depression

It is a more common type of depression.it is not typical type of depression .over eating, sleep too much, fatique, weakness and sensitivity to rejection are the symptoms of depression. Monoamine oxidase inhibitor (MAOI) is a type of antidepressant which shows better respond to atypical depression**.**

Pathophysiology

The Pathophysiology of depression theories are explained on the basis of different types of hypothesis. Depression studies are being unclear due to the difficulty in the availability of human brain tissue for neurochemical measurement in post mortem .The Normal physiology of depression focuses mainly on neurotransmitters in the brain[4]. There are around 46 neurotransmitters and they were playing more than one function. The Neurotransmitters are chemical messenger to transmit messages between neurons, or from neurons to muscles with in the nervous system. They use electrical signals to stimulate messages from the neuron to

the target cells. These neurotransmitters are released from the synaptic vesicles into synaptic cleft and they are collected by the neurotransmitter receptors in the target cell.

Studies are shown that depression is associated with decrease in the level of serotonin (5-HT) in the brain. Serotonin is one of the important neurotransmitter that regulates various functions such as sleep, appetite, happiness, anxiety, energy balance etc. The Norepinephrine is another neurotransmitter that helps regulates mood, alertness etc and also helps respond in stressful situations. Dopamine is another important neurotransmitter in the brain that helps in motivation in which people have loss of interest in activities caused by the depression and helps to take actions. Sufficient levels of Neurotransmitters are necessery for the proper functioning of brain.

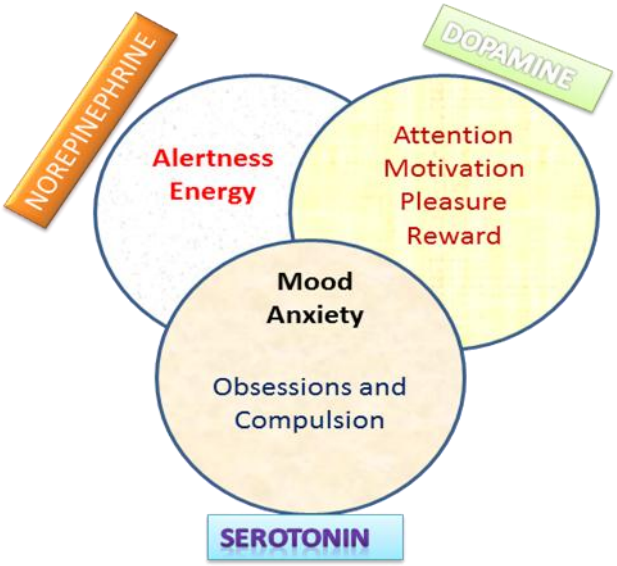

Figure 2: Pathophysiology of depression.

The Pathophysiology of mood disorder or depression is yet unclear. The research studies are continueing. But different types of theories are there,

Genetic Predisposition and Environmental influences

There is lot of evidence from the twin, family and adoption studies that the major depression is a familial disorder and this is due to the genetic factors. Nowadays important studies are suggest that the familial environment risk factors and the parental social behavior are not as important in the pathogenesis of depression as previously assumed. Above studies are suggest that genetic factors influences the depression around 30-40%. The remaining 60-70 % are influenced by non genetic factors .There will be more chances to develop major depression in

Individuals with 2 copies of the s allele than individuals homozygous for the l allele. The mood disorders have connection between environmental influences and susceptible genes. There will be combination of life stressors and potentially dysfunctional serotonin system. The serotonin transporter causes in the reuptake of serotonin at the synapse and they moderate serotonergic response to stress. The stresses may be adverse events in childhood and recent or ongoing stress due to childhood sexual abuse, lifetime trauma, marital problems, divorce and low social support etc. in depression the stress sensitivity is partly gender specific. Both men and women are equally sensitive to depressogenic effect of stressful life events and may vary depending on the type of stressor. The studies are states that the men are more likely to have depressive episodes because of divorce and work difficulties, while the women are more sensitive to depression because of serious illness and difficulty in getting alone with an individual.

Neurochemical dysregulation

Monoamine hypothesis

Monoamine hypothesis is the first major hypothesis of depression was formulated about 30 years ago. This hypothesis suggest that the main symptoms of depression are due to functional deficiency of of the brain monoaminergic transmitters such as norepinephrine (NE), serotonin (5-HT) and dopamine. The Antidepressant drugs are mainly focusing on increasing the monoamine neurotransmitter levels within the brain.

Neuroendocrine dysregulation

The pathophysiology of depression includes 2 theories that involve dysregulation of the neuroendocrine system.in the first one focuses on stress and hypothalamus-Pituitary-adrenal system. The HPA system plays an important role in the pathophysiology of depression. Thedysregulation in the HPA axis due to depression results in increased corticotropic releasing factor (CRF) from the hypothalamus, enlarged adrenal gland &they causes increased secretion of cortisol (Glucocorticoids). The increased cortisol release in the body results in the secretion of pro-inflammatory cytokines which causes immunosupression and inflammation.

In the second neuroendocrine dysregulation is in Hypothalamus-pituitary-thyroid (HPT) system. About 20-30% of cases of depression have shown the dysregulation in hypothalamic-pituitary-thyroid (HPT) system. Because of this dysregulation there is an increase in

thyrotropin releasing hormone and also increase in thyroid stimulating hormone. this all increase the risk of depression.

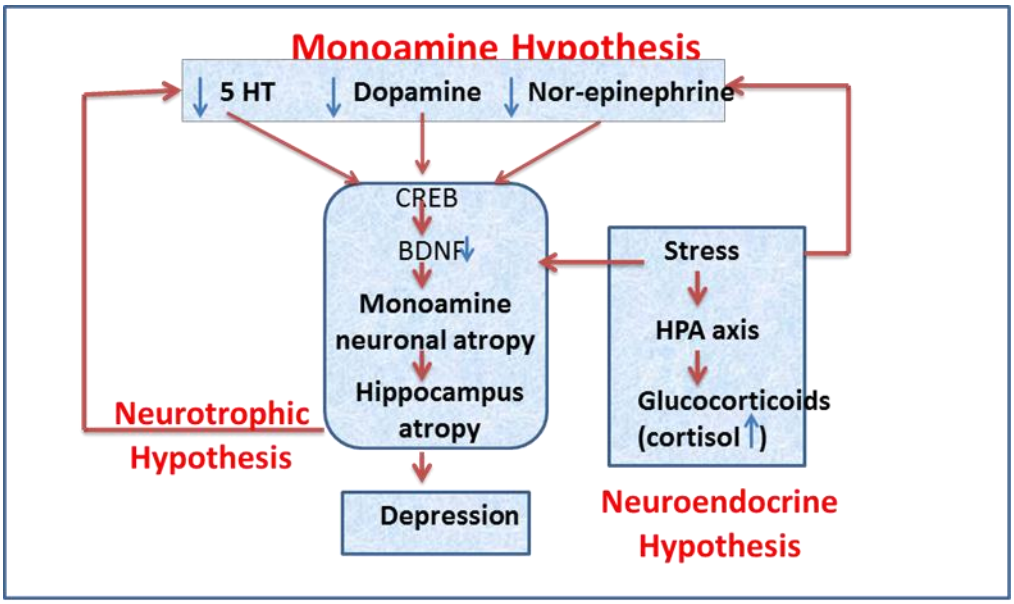

Figure 3: Neurochemical dysregulation.

Neurotrophichypothesis of depression

In the neurotrophic hypothesis suggest that the depression may be associated with drop in Brain derived neurotrophic factor (BDNF) level. Brain derivedneurotrophic factor (BDNF) is a factor that promotes the growth and development of immature neurons including monoaminergic neurons and also that enhances the survival and function of adult neurons. The low BDNF level may be responsible for loss of monoaminergic neurons and loss of function or atrophy of hippocampus and other brain areas. At that time hippocampus lose its ability to inhibit CRF release by hypothamus leading to increased release of glucocorticoids(cotisol).

Neuroanatomic and Function abnormalities

In depressed individuals the post mortem result have shown the decrease in 5 HT 1 a receptor subtype binding in the temporal, frontal , limbic cortex and also serotonin transporter binding in hippocampus and cerebral cortex that shows a dysfunction in the raphe-serotonin system. The locus ceruleus-norepinephrine system activation causes inhibition of raphe-serotonin system. This suggest an indirect modulating function of serotonin. In Some of the suicide victims of depression Norepinephrine receptor alteration are found in the frontal cortex.

These alteration in the NE system that may shows attention or concentration difficulties and also sleep disturbances in depression. In people with unipolar disorder they shows a decreased number of glial cells in the frontal and limbic region as well as, low frontal lobe volume and low prefrontal cortex functioning. The individuals with depression have also been found to have cerebral blood flow abnormalities and glucose metabolism. Depressed individuals with dorsolateral prefrontal abnormalities may be responsible for speech difficulties and also cognitive processing retardation similar to those found in schizophrenia.

Pharmacologic treatment

Depression is a serious neurological disorder but it's also treatable. There are different types of treatment for depression that include Self-help such as Regular exercise, spending time with people who care about you etc., Psychotherapy or counseling, Alternative medicine such as massage, acupuncture, hypnosis and brain stimulation therapy such as electroconvulsive therapy (ECT), electroconvulsive therapy (ECT), transcranial magnetic stimulation (TMS) and vagus nerve stimulation (VNS).

Antidepressants are the prescription medicine which is given for depression that reduce the symptoms of depressive disorder by altering the chemical imbalances of neurotransmitters in the brain. Generally in people with depression the availability of neurotransmitters such as serotonin, nor epinephrine or dopamine is characterestically low in the brain. The antidepressants are work by increasing the availability of one or several of those neurotransmitter. Neurotransmitters are the communication link between nerve cells they are found in vesicles of the nerve cells, it is released by one nerve and picked up by another nerve. There are different types of antidepressants. they are;

1. **Tricyclic antidepressants (TCAs)**

Tricyclic antidepressants are the class of drug which is used for depression. They are so named because in the chemical structure they contain 3 rings.[4] They are mainly used to treat anxiety, depression and help to control chronic pain. These drugs are act by blocking the reuptake of serotonin & nor epinephrine into the nerve cells.eg:-Imipramine, Descipramine, Amitriptyline.

2. **Selective serotonin reuptake inhibitor (SSRI)**

Selective serotonin reuptake inhibitor are the commonly prescribed antidepressants drugs. They are act by selectively inhibiting or blocking the reuptake of serotonin and those having fewer side effects than the other antidepressants.eg:- Citalopram, Fluxetine, Paroxetine.

3. Serotonin/nor epinephrine reuptake inhibitor (SNRI)

Selective serotonin reuptake inhibitor an important class of drug used to treat major depression, mooddisorder, anxiety disorders and chronic neuropathic pain. SNRIs are mainly act by inhibiting the reuptake of both norepinephrine and serotonin.eg:- Duloxetine, Venlafexine and Desvenlafaxine.

4. Monoamine oxidase inhibitor (MAOIs)

Monoamine oxidase inhibitors are the commonly prescribed drug for depression. These are act by inhibiting the action or activity of monoamine oxidase enzyme and there byincreasing the concentration of neurotransmitters in the brain. Eg:-phenelzine, tranylcypromine, isocarboxazid and selegiline. These drugs should not be combined with other antidepressants or other drugs that will increase serotonin levels (for eg:- amphetamines, linezolid).these combinations cause excessive serotonin levels in the brain, which may lead to confusion, high blood pressure etc.

The long term use of the synthetic antidepressant drugs have reported many side effects such as addiction, blurred vision, urinary retention, hypertension, abnormal heart rhythm, insomnia, sexual dysfunction, nausea, vomiting, dizziness, psychosis, suicidal thinking, seizures etc. the side effects of the antidepressants which can be averted to large extend by herbal drug. Herbal medicines become an item of global importance both medical and economical. Recently considerable attention has been paid to utilize ecofriendly and biofriendly plant based products for the prevention and cure of various human diseases. The herbal medications have better patient compliance as they devoid of typical side effects of allopathic medication. Traditionally large number of herbal formulation are used for the treatment of depression.

There are many herbal drug for antidepressant activity. include, *Asparagus racemosus, Curcuma longa, Ginkgo biloba, bacobamonnieri, Clitiriaternatea, Mimosa pudica, Mimosa pudica.*[7] Here the selected herbal drugs are roots of Ashwagandha(*Withaniasomnifera)* and seeds of Velvet bean (*MucunnaPruriens).*

Ashwagandha (*Withania somnifera)*

It consist of dried roots of *Withania somnifera* belongs to the family *Solanaceae*.It is a small evergreen shrub of 200-800 cm height. It is an important medicinal herb used in the traditional system of medicine, for more than 2000 years for the ailment of different kinds of diseases. it is commonly called as “indian winter cherry” and “ Indian ginseng”.[9]

Figure 4: Ashwagandha plant. Figure 5: Roots of ashwagandha.

Ashwagandhais an evergreen, erect, branching shrub and found throughout in the drier areas of India, Bangladesh, Sri-lanka, Nepal and other parts of Africa, America and Australia. In india it is seen in the region of Madhya Pradesh, Uttar Pradesh, Gujarat, panjab and Rajasthan. leafs of ashwagandha are simple, petiolate with leaf blades. Leaves are alternate and large and floral branches are opposite and arranged laterally in pairs of one small and one large leaf. it is probably occure in the drier and humid areas and it is mainly spread from the Mediterranean region to tropical region of Africa, South Africa, Arabia and Middle east region like India, China and Sri lanka. It is propagated and cultivated in the warmer and drier regions in gardens of Europe. In india it is generally cultivated for its fleshy roots as a medicinal crop. Flowers are small, greenish, axillary, monoceous and solitary or in few flowered cymes. It produces pale green monoceous flowers in all the year with a peak of flowering in between March and July. Seeds are yellow or white in color, numerous, laterally compressed and tomentose at the apex which is covered with minute stellately hairs. The Roots are fleshy in dried form and they are straight, cylindrical, tapering down and whitish brown in color.[28]

Ashwagandha act as an important ingredient in many ayurvedhic formulation. Ayurvedhic formulation containing *withania somnifera* which is prescribed as analgesic for a variety of musculoskeletal disorders such as Arthritis and Rheumatism, for stimulating sexual impulses and increases sperm count,certain forms of hypertension. In ancient times it is used as nerve tonic, aphrodisiac, adaptogen, antirheumatic agent, astringent and also memory enhancer. To describe multiple biological properties of ashwagandha many pharmacological studies have been carried out and outcomes from those studies indicate that it is also used to treat asthma, ulcer, cancer, insomnia, senile dementia and bronchitis. It is also used as antidiabetic,

immunomodulatory, hemopoitic, neurological inflammatory disorders and parkinson's disease which are supported by different preclinical and clinical trials.it is mainly act as a potentially useful adjunct for patient receiving radiation and chemotherapy because of its chemopreventive properties. It is also act as antibiotic, antioxidant, deobtruent, abortifacient, diuretic and sedative. It act as a powerful adaptogen so that it enhances body's resilience to stress and also it improve body's defense against disease by enhancing cell mediated immunity. W. Somnifera showing potent antioxidant activity that help to protect cells from damage that caused by free radicals.

The laboratory analysis revealed that *W. Somnifera* root contained over 35 chemical constituents. The roots of *W. somnifera* primarily compossed of compounds known as withanolides, which are mainly account for its medicinal properties. Withanolides are steroidal lactones which is showing resemblance with the active constituents of asianginseng (panax ginseng) both in action and appearance known as ginsenosides. SK Bhattacharya *et al* (1987)Presented a study on Ashwagandha. It enhances the function of the brain and nervous system and improves the memory. Sitoindosides and acylsterylglucosides in Ashwagandha are anti-stress agents. The sitoindosides VII-X andWithaferin-A, have been shown to have significant anti-stress activity against acute models of experimental stress.

Constituents present

The biologically active constituents of *withania somnifera* are

- Alkaloids: Isopellertierine, Anaferine, Anahygrine, Cuscohygrine, Somniferinine, Somniferiene, Tropanol, Withanine, Withananine.
- Steroidal lactones: Withanolides, Withaferine
- Saponins containing acyl group: SitoindosideVII and VIII
- There are two main withanolidesthat are withaferin A and withanolide D

The important chemical constituents of W. Somnifera are withanolides, these are steroidal lactones which containing ergostane skeleton. The toxicological studies and data obtained from various research works was demonstrated that the ashwagandha plant is non toxic in a range of practical doses. Except these the plant also contain various chemical constituents such as starch, reducing sugar, withaniol, acyl sterylglucosides, hantreacotane, ductol etc. it also contain variety of aminoacid like aspartic acid , proline, tyrosine, alanine, glycine, glutamic acid, cystine, tryptophan and high amount of iron.W. Somnifera usually given as a powder form as churna, liquid form as tonic, semisolid form like lehya.

Velvet beans (*Mucunapruriens)*

It consist of dried seeds of *Mucuna Pruriens* belong to the family *Fabaceae*. The velvet bean plant is a climbing shrub with long vines and that can grow over 15 meters in length and which has long been used as a traditional ayurvedic medicine for diseases such as parkinsonism.[10] It is commonly called as monkey tamarind, velvet bean, cowitch, lyon bean and Mauritius velvet bean. The plant on contact produces extreme itchiness, especially with the seed pods and young foliage.

Figure 6: Velvet bean plant.

Figure 7: Seeds of velvet bean.

M. pruriens is native to tropical or subtropical regions, but can also adapt to well-drained, sandy soils as well as clay soils. The plant is almost covered with fuzy hairs, when the plant is young.

When the plant is older, it is completely free of hairs. The leaves are tripinnate, ovate, rhombus shaped. The tips of leaves are pointy and the leaf sides are often heavily grooved.

M. Pruriens contain lavender, white or purple coloured flowers. it contain 10-20 cm long pods and that are covered with white to creamish hairs that causes extreme itching if they come in contact with skin .itch is mainly responsible due to chemical compounds such as protein, mucunain and serotonin. The fruits are unwinged, leguminous, and they have a ridge along the length of the fruit. The husk of the fruit is very hairy and carries around seven seeds.it is about 13 cm long and 2 cm wide. The seeds are dark brown in color and thickly covered with stiff hairs. In olden times *M. pruriens* plants are widely cultivated as a green vegetable crop and it was originally from eastern india and southern china. In some countries it has been traditionally used as a food source. *M.pruriens* plants are cultivated in Asia,

Africa, America and also in pacific Islands, its pods are used as a vegetable and its leaves are used as animal food.

M. pruriens is well known Indian medicinal herb, which has been used as a traditional medicine long year back. In ancient time also it is used for various ailments. It is mainly used to treat nervous disorders, arthritis and also it is also employed as a powerful aphrodisiac.[11] In ancient times, the bean is applied as a paste on scorpion stings, because it thought to absorb the poison.it is mainly used to treat Parkinson's disease because of the presents of L-dopa. Levodopa is an important neurotransmitter precursor, it is believed to be responsible for the toxicity. It is also shows anti-neoplastic activity and also anti-epileptic activity. It is also act as potent anti-oxidant and anti-microbial agent. Various parts of the *M. pruriens* contain valuable medicinal properties, it incudes anti-diabetic, aphrodisiac, anti-venom,anti-helminthic, analgesic and also anti-inflammatory activity.

Mucuna pruriens seed have been reported to contain toxic compounds such as L-dopa and anti-nutritional factors such as tannins, phenols and tryptamine with hallucinogenic effect.is also used for the treatment of Parkinson's disease because of the high concentration of L-dopa. Due to the presents of some sulfur containing amino acids they producing anti-physiological and toxic factors that may contribute to decrease in their overall nutritional effects. M. pruriens contains various factors such as lectins, alkaloids, polyphenols, trypsin inhibitors, phytate, oligosaccharides, cyanoglycosides and saponin.[12] Now a days, studies are suggest that Phenolics or phenolic compounds are responsible for the anti-microbial, anti-inflammatory, hypotensive, anti-carcinogenic and also for anti-oxidant activities. Cynogenic glycosides are a type of toxin which present in plants on hydrolysis they liberate hydrogen cyanide, it is known cause for acute and chronic toxicity.

Constituents present

Mucuna pruriens seedas contains various phytoconstituents, which are responsible for various effects.

- The *Mucuna pruriens* seeds contains about 3-6% Levodopa.
- Alkaloidal constituents like mucunine, prurienine, mucunadine, prurienine
- Epoxy fatty acids such as cis-12, 13-epoxyoctadec-trans-9-cis-acid,cis-12,13-epoxyoctadectrans-9-enoic acid.

- It contains many diverse phytochemicals like 1-methyl-3-carboxy-6, 7-dihydroxy-1,2,3,4-tetrahydroisoquinolone,5-hydroxy tryptamine, 5-methoxy-n,n-dimethyltryptamine-noxide, 5-oxyindole-3-alkylamine, alanine, arachidic acid, arginine, aspartic acid, behenic acid, β-carbolineβ -sitosterol, bufotenine, choline, cystine, leucine, linoleic acid, myristic acid, n,n-dimethyltryptamine-n-oxide, nicotine, oleic acid, palmitic acid, palmitoleic acid, phenylalanine, phosphorus, proline, protein, saponins, serine, stearic acid, threonine, tryptamine, tyrodine, valine and vernolic acid.
- It contains oligosaccharide such as verbascose.

Sachchida Nand Rai *et. Al* (2018) indicated that Levodopa is the only gold standard medication used since long time but it causes several side effects like drug induced dyskinesia. Natural compound and herbal extract like Mp and Ws shows strong and potential neuroprotective activity in chemical induced PD mice model. In addition the synergistic effect of Mp and Ws show effective neuroprotective activity. A lot of clinical trial has been done on herbal extract and their isolated compound in order to patent the drug. An Ayurvedic treatment of *mucuna pruriens* and *withania somnifera* they exhibit better efficacy alone or in combination without causing any side effect.[19]

Extended release dosageform

An extended release dosageform are defined as one that allows a reduction in dosing frequency. To that presented by a conventional dosage form. Extended release dosage form are those which release drug slowly, so that the plasma concentrations are maintained at a therapeutic level for a prolong period of time usually between 8-12hrs.[30] Extended release produce are designed to release their medication in a controlled manner, at predetermined rate, duration and location to achieve and maintain optimum therapeutic blood levels of drug. They extended release medication when swallowed, it begins working to relieve pain in about 2 to 4 hrs and it attains its peak effect in 15 to 30 hrs. It will continue to work for a few days. This type of drug is designed to produce a long acting study rate of pain relief.

Advantages

- An important advantage of extended release dosage form is that it reduce the dosing frequency and provide long action of the drug.
- It reduces the necessary of night time doses that helpful for both patient and bystander.

- There is no need of repeated consumption of tablet and capsule, which is useful for children and old people.
- By controlling the rate of drug release it can be used to maintain drug levels.
- It may improve patient compliance.
- The rate and extend of medicament absorption can be improved.
- The dosage form is already coated with granules so that there is no problem the un pleasant taste and odour of the drug.
- It reduced the side effect, reduce the time required for health treatment and also improves medical benefit.
- They are easy to carry and transport.
- It releases the medicament at a prescribed rate as per the needs of the body throughout the treatment of patient.

Disadvantages

- The high cost of this formulation is the major disadvantage of extended release dosage form this is because of the high manufacturing cost compared to other dosage form.
- The side effect can be reminds longer than immediate release dosage form.
- It is not suit whenever partial doses are needed because they need to be taken intact, not divide in to parts.
- The release property lost whenever the medication is divided in to parts.
- It may cause slower onset of action.
- The factors such as food and fasting can change the release rate.
- For this formulation release rate can vary from one dose to another dose.

CONCLUSION

The long term use antidepressant drugs have reported many side effects which can be averted to large extend by herbal drugs. based on review of literature the herbal medicinal drugs posses better action with lesser side effects. Natural compound and herbal extract like Mp and Ws shows antisress activity and neuroprotective activity in mice model. synergistic effect of Mp and Ws show effective Antistress activity. the ayurvedic treatment of mucuna pruriens and withania somnifera they exhibit better action alone or in combination without causing any side effect.

REFERENCES

1. Ksithija Iyer. Depression– A Review. Research Journal of Recent Sciences, 2012; 1(4): 79-87.
2. Jonathan W Kanter, Andrew M Busch, Cristal E Weeks, Sara J Landes. The Nature of Clinical Depression: Symptoms, Syndromes, and Behavior Analysis. Behav Anal, 2008; 31(1): 1–21.
3. Franco Benazzi. Various forms of depression. Dialogues Clin Neurosci, 2006; 8(2): 151–161.
4. Todd M. Hillhouse, Joseph H. Porter. A brief history of the development of antidepressant drugs: From monoamines to glutamate. Exp Clin Psychopharmacol, 2015; 23(1): 1–21.
5. Bondy brigitta. pathophysiology of depression & mechanism of treatment. Dialogues in clinical Nueroscience, 2002; 4(1): 7-20.
6. Narendra Singh, Mohit Bhalla, Prashanti de Jager,* and Marilena Gilca. An Overview on Ashwagandha: A Rasayana (Rejuvenator) of Ayurveda. African Journal of Traditional, Complementary and Alternative Medicine, 2011; 8(5): 208–213.
7. Talha Jawaid, Roli Gupta and Zohaib Ahmed Siddiqui. A Review on herbal plants showing antidepressant activity. International Journal of Pharmaceutical Sciences and Research, 2011; 2(12): 3051-3060.
8. Lakshmi-Chandra Mishra, Betsy B. Singh.Scientific Basis for the Therapeutic Use of Withania somnifera (Ashwagandha): A Review. Alternative Medicine Review: a Journal of Clinical Therapeutics, 2000; 5(4): 334-46.
9. Jayanthi. MK, Prathima. C, Huralikuppi, suresha jc and Murali Dhar. International Journal of Pharma and Bio Sciences Anti-Depressant effects of *withania somnifera* fat (Ashwagandha ghrutha) extract in experimental mice, 2012; 3(1): 33-39.
10. Digvijay G. Rana, Varsha J. Galani. Pharmacological Study Dopamine mediated antidepressant effect of *Mucuna pruriens* seeds in various experimental models of depression. AYU Journal, 2014; 35(1): 90-97.
11. Kavitha.k.Evaluation of total phenols, total flavanoids, Antioxidant, and Anticancer activity of *mucuna pruriens* seed extract. Asian journal pharmaceutical and clinical research, 2018; 11(3): 242-246.
12. A. Pinna, S. Pontis, N. Schintu, N. Simola, S. Kasture, Morelli M. Assessment of symptomatic and neuroprotective efflcacy of *Mucuna pruriens* seed extract in rodent model of Parkinson's disease. Parkinsonism & Related Disorders, 2009; 15(2): 117.

13. Bhattacharya SK and Bhattacharya D. Effect of restraint stress on rat brain serotonin. Bioscience, 1982; 4(3): 269-74.
14. Adell A, Casanovas JM, Artigas F. Comparative study in the rat of the actions of different types of stress on the release of 5-HT in raphe nuclei and forebrain areas. Neuropharmacology, 1997; 36: 735-41.
15. Penalva RG, Flachskamm C, Zimmermann S, Wurst W, Holsboer F, Reul JMHM. Corticotropin releasing hormone receptor type-I deficiency enhances hippocampus sertonergic neurotransmission: an in-vivo microdialysis study in mutant mice. Neuroscience, 2002; 109(1): 253-66.
16. Bhattacharya A, Ghosa S, Bhattacharya SK. Anti-oxidant effect of *Withania somnifera* glycowithanolides in chronic foot shock stress-induced perturbations of oxidative free radical scavenging enzymes and lipid peroxidation in rat frontal cortex and striatum. J Ethnopharmacol, 2001; 74(1): 1–6.
17. Shobhit Singh, Pushpraj .S Gupta, ishikesh Gupta. Evaluation of anti anxiety activity of *Mucuna pruriens*. Journal of Drug Delivery and Therapeutics, 2019; 9(4-A): 104-107.
18. Bhattacharya SK, Muruganandam AV. Adaptogenic activity of *withania somnifera*: an experimental study using a rat model of chronic stress. Pharmacology Biochem Behav, 2003; 75(1): 547–55.
19. Sachchida Nand Rai, Hareram Birla, Walia Zahra, Saumitra Sen Singh and Surya Pratap Singh. The Role of *Mucuna Pruriens* and *Withania Somnifera* in the Neuroprotection and Treatment of Parkinson's disease. SOJ Neurology, 2018; 5(1): 1-6.
20. Pratap Singh S, Nand Rai S, Hareram Birla. The Role of *Mucuna Pruriens* and *Withania Somnifera* in the Neuroprotection and Treatment of Parkinson's disease. SOJ Neurol, 2018; 5(1): 1-6.
21. Mithun Singh, Sampada Sinha, Vineet Mathur, Purti Agrawal. Herbal Antidepressants. International Journal of Pharmaceutical Frontier Research, 2011; 1(1): 159-169.
22. Sanjay Kumar Gupta, Afra Huneza, Sradhajali Patra. Formulation, Development and *in vitro* Evaluation of Tramadol Extended-Release Tablets. Int J Pharm Pharm Sci, 2019; 11(7): 63-73.
23. Chilvalyar sapnil, Vuma maheshwara Rao, P Vishnu, G Ashok, B Ajay kumar. Formulation and evaluation of extended release tablets of Tramadol Hydrochloride. International Research journal of Pharmacy, 2013; 7(1): 65-68.
24. Margret Chandira, B.S.Venkateswarlu, JadhavAnup Shankar rao, Debjit Bhowmik, B. Jayakar, T. V. Narayana. Formulation and Evaluation of Extended Release Tablets

containing Metformin HCl. International Journal of Chem Tech Research, 2010; 2(2): 1320-1329.

25. Snehal S. Patel, Niti Rajshree, Praboth V. Shah. Evaluation of Antidepressant Activity of Herbomineral Formulation. International Journal of Pharmacy and Pharmaceutical Sciences, 2016; 8(4): 145-147.
26. Mamatha Thirunagari, Anupama Koneru, Mohd Abdul Hadi, Husna Kanwel Qureshi. Formulation Evaluaion of Extended Release tablets of an Antidepressant drug Venlafaxine Hcl. International journal of Research in Pharmaceutical sciences, 2018; 9(4): 1146-1153.
27. Michal Horowitz. Antidepressant and anxiolytic-like, sedation and hypnosis. J Basic Clin Physiol Pharmacol, 2017; 28(2): 91–92.
28. Naveen Gaurav, Dr. Arun Kumar, Dr. Manjusha Tyagi, Deepak Kumar, Dr. U.K. Chauhan, Prof. A. P. Singh. Morphology of Withanisomnifera (Distribution, Morphology, Phytosociology of Withania somnifera L. Dunal), 2015; 1(7): 164-173.
29. Princy Agarwal, Rajat Vaishnav & Anju Goyal. Comparative Quality Evaluation of Three Different Marketed Brands of Ashwagandha Churna (Powder). Global Journal of Medical Research, 2018; 18(3): 13-23.
30. Sachiko Fukui, Hideki Yano, Shuichi Yada, Tsuyoshi Mikkaichi, Hidemi Minami. Design and evaluation of an extended-release matrix tablet formulation; the combination of hypromellose acetate succinate and hydroxypropylcellulose. asian journal of pharmaceutical sciences, 2017; 12(1): 149–156.