IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

COMPARATIVE STUDY OF HERBAL ANTIDEPRRESENT OVER THE MODERN MEDICINE

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ABSTRACT:

A mental health disorder characterized by persistently depressed mood or loss of interest in activities, causing significant impairment in daily life. Possible causes include a combination of biological, psychological and social sources of distress. Increasingly, research suggests that these factors may cause changes in brain function, including altered activity of certain neural circuits in the brain. This is the most common in the India because more than 10 million cases per year are observed here.

KEY WORDS

Efficacy, safety, quality control, marketing and regulatory guidelines for herbal medicines (phototherapeutic agents) and Antidepressants.

INTRODUCTION

Antidepressants are medications used to treat major depressive disorder, some anxiety disorders, some chronic pain conditions, and to help manage some addictions. Common side-effects of antidepressants include dry mouth, weight gain, dizziness, headaches, sexual dysfunction, and emotional blunting. Most types of antidepressants are typically safe to take, but may cause increased thoughts of suicide when taken by children, adolescents, and young adults. A discontinuation syndrome can occur after stopping any antidepressant which resembles recurrent depression.

DEPRESSION:

An illness that involves the body, mood, and thoughts and that affects the way a person eats, sleeps, feels about himself or herself, and thinks about things. Depression is not the same as a passing blue mood. It is not a sign of personal weakness or a condition that can be wished away. People with depression cannot merely 'pull themselves together' and get better.

Types of depression

1. Major Depression
2. Premenstrual Dysphoric Disorder (PMDD).
3. Seasonal Affective Disorder (SAD)
4. Bipolar Disorder
5. Anti-natal & Post-natal Depression
6. Psychotic Depression
7. Persistent Depressive Disorder (Dysthymia)

ANTIDEPRESSANTS

DEFENATION

These are a class of drugs that reduce symptoms of depressive disorders by correcting chemical imbalances of neurotransmitters in the brain. Chemical imbalances may be responsible for changes in mood and behavior.

TYPES OF ANTIDEPRRESENTS

- Selective serotonin reuptake inhibitors (SSRIs) ...
- Serotonin-noradrenaline reuptake inhibitors (SNRIs) ...
- Noradrenaline and specific serotonergic antidepressants (NASSAs) ...
- Tricyclic antidepressants (TCAs) ...
- Monoamine oxidase inhibitors (MAOIs)

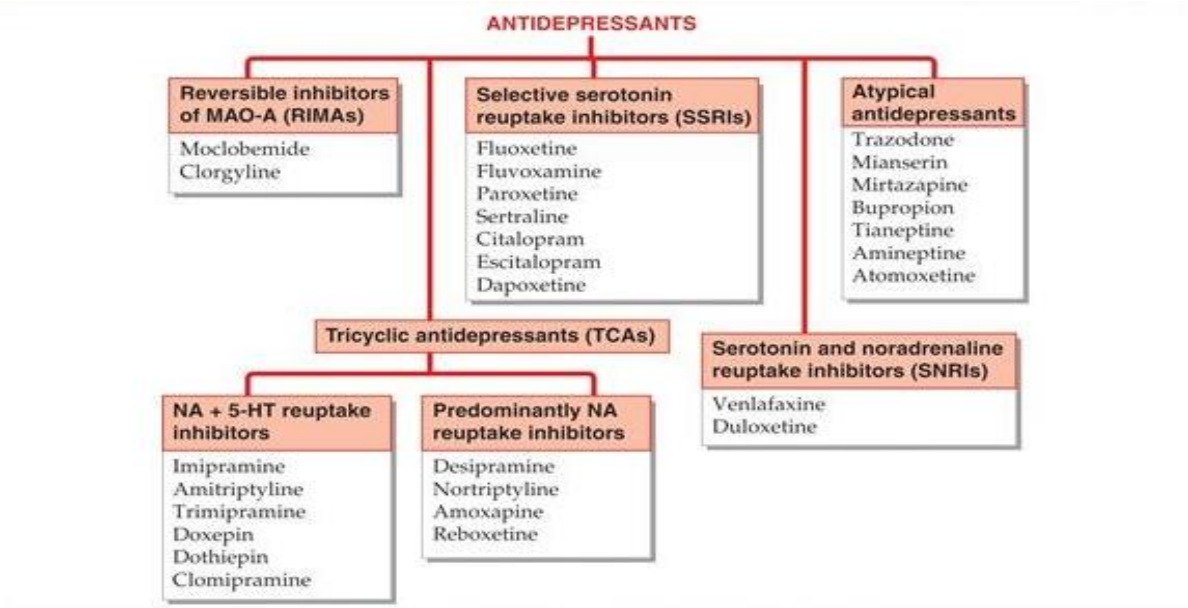
ADVANTAGES OF ANTIDEPRESSENT

1. LESS SEDATION
2. ONSET IS FAST
3. LONG DURATION
4.WIDE SAFETY MARGIN

DISADVANTAGES OF ANTIDEPRESSENT

1.NAUSEA
2.INSOMNIA
3. DRY DMOUTH
4. BLURED VISION

CLASSIFICATION OF ANTIDEPRESSENT



GENERAL MECHANISM OF ACTION OF ANTIDEPRESSENT

- Inhibit the re-uptake of neurotransmitters.
- They inhibit serotonin,nor epinephrine or dopamine reuptake at pre synaptic nerve terminals thus lead to increased concentration of these transmitters in the synaptic cleft.
- Takes up to 4 weeks for all TCA antidepressants to have an effect.

MEDICINES USED AS ANTIDEPRESSENT

1.HERBAL MEDICINES
2.MORDEN MEDICINES

HERBAL MEDICINES

1. BRAHMI
2. SHANKPUSHPI
3. JYOTISHMATI
4. HYPSERICUM PERFORATUM
5. TULSI
6. ASHWANGANDHA
7. GINSENG
8. LAVENDER
9. JASMINE
10. RHODIOLE
11. CHAMOMILE
12. SAFFRON
13. PEPPERMINT
14. JASMINE
15. ALOE VERA
16. MULITHI

1.BRAHMI (BACOPA MONNIERI):

Name: Brahmi, Bacopa monnieri, Herpestis monniera, Indian pennywort, Water hyssop
Active Compounds: Bacosides, Bacopasaponins

Pre-clinical studies suggest that Bacopa extracts have antidepressant property. However, Brahmi is a proven natural cognition enhancer and its use (as an add-on therapy) during depression recovery or remission may help counteract cognitive deficits occurring in MDD.TULSI (OCIMUM SANCTUM)

Bacopa lowers depression and anxiety symptoms

Studies in animal models have confirmed that Bacopa monnieri extracts have antidepressant activity comparable to a conventional antidepressant, imipramine.
This antidepressant action could be a result of changes in brain chemistry and antioxidant action of the herb.

Pre-clinical evidence suggests that bacosides influence multiple neurotransmitters in the brain- serotonin, GABA, glutamate, catecholamine, acetylcholine.
Bacopa monnieri is an adaptogen. Its anti-stress action is similar to that of ginseng. It normalizes stress hormone levels and restores the activity of neurotransmitters serotonin (our happy hormone), dopamine and noradrenaline.

Depressive symptoms are associated with increased oxidative stress (an imbalance between prooxidant and antioxidant agents). Supplementation or a diet rich in antioxidants can help counteract oxidative stress in the brain and prevent depression progression.

Liu and colleagues have demonstrated that bacopaside I mediate antidepressant effect primarily by boosting antioxidant defences in the brain and activating systems related to our brain chemistry.

HPA axis or hypothalamic pituitary adrenal axis is an interaction between part of the brain and adrenal glands that play an important role in our stress response. It regulates our stress hormone-cortisol levels. A recent study published in Neurochemical research, 2017 revealed that bacopaside I normalises HPA axis function and lowers cortisol levels in stressful conditionons. It increases resilience to stress by supporting neuroplasticity or the ability of our brain to adapt to changes and rewire itself. This was evidenced by an increase in BDNF or Brain-Derived Neurotrophic Factor (a protein essential for growth and development of neurons), which is otherwise reduced during stress and depression .

Bacopa monnieri can protect memory and cognition in depression

A recent study (on an animal model) published in Metabolic Brain Disease highlights how high levels of stress hormone and chronic stress can induce severe depression with cognitive deficits such as altered learning and memory issues. It leads to disruption of neurotransmitter activities that are involved in memory formation and storage. Cognitive impairments in depression may present as errors in calculations, reduced working memory, impaired verbal fluency, reduced focus and poor performance on other cognitive tasks. Apart from depression pathology, certain antidepressants may also cause cognitive blunting. Bobinska et al. have identified a link between neuroinflammation and cognitive deficits. Expression of genes controlling inflammatory processes is found to influence certain cognition related parameters such as verbal fluency, learning, working memory and attention. Considering that Brahmi naturally relieves neuroinflammation (inflammation in the brain), it may also serve as a cognition enhancer. In fact, its cognition-enhancing activity is the prime reason why researchers are studying its constituents and their possible use as a nutraceutical for attenuating cognitive decline and dementia. As I mentioned earlier, bacoside A is the principal active constituent of Brahmi that influences brain health positively. A study published in PLoS One, 2015 demonstrated that bacosides do not effectively bind to receptors in the brain but secondary metabolites and derivatives obtained from bacosides effectively bind to receptors, are well observed from the intestine and effectively cross Blood Brain Barrier. The researchers stated that bacoside A aglycones and its derivatives are responsible for its cognition-enhancing activity. Animal studies indicate that Brahmi extracts interact with neurotransmitter systems and support neuroplasticity to ameliorate memory issues in depression.

It can lower inflammation and oxidative stress in the brain in depression

Inflammation plays an important role in development and progression of depression. It is accompanied by oxidative-nitrosative stress where there is a decline in natural antioxidant defences in the brain and reactive oxygen and nitrogen species cause oxidative damage. Major life stressors, social threat, adversity and rejection, poor diet, physical inactivity, obesity, smoking, vitamin D deficiency, poor gut health is few of the causative risk factors for inflammation in depression. Bacopa monnieri extracts prevent activation of microglial cells (immune cells of the central nervous system) and inhibit release of pro-inflammatory agents such as Tumor Necrosis Factor-alpha and Interleukin-6 in the brain cells.

2.SHANKPUSHPI (CONVOLVULUS PLURICAULIS)

Shankhpushpi, clad by the vernacular names Shankhini, Kambumalini, Samkhapushpi, Sadaphuli, and Sankhaphuli is a potent memory booster and brain tonic that actively works to improve intelligence and functioning of the brain. The name shankhpushpi was given to the plant owing to its shankh or conch shaped flowers. It also helps in enhancing concentration, learning capabilities, mental fatigue, insomnia, stress, anxiety, depression, etc It improves mental health and might help in managing depression due to its antidepressant activity.
According to Ayurveda, Shankhpushpi helps to calm down the brain and relieve stress as well as anxiety. It also improves memory by acting as a brain tonic due to its Medhya (improves intelligence) property. You can take Shankhpushpi powder along with warm milk or water to help boost memory and concentration. Shankhpushpi tablets and capsules can also be used to improve brain functions.
Shankhpushpi Syrup is an ayurvedic remedy for memory and brainpower. It is beneficial in mental weakness, forgetfulness, memory loss, low retention power etc. However, medicines or supplements can only improve alertness, attention span, brain functions, nerve coordination and brain's retention capability, but these supplements may not change your habits of procrastination. Therefore, daily brain exercises are also required to boost brain capabilities. capabilities. In Ayurveda, Shankhpushpi has been given the status of a nerve tonic. The reason is that it contains elements such as tryptanoids, flavonol glycosides, anthocyanins, and steroids.

Boosts Cognition And Memory

As a memory-boosting remedy, shankhpushpi powder is combined with milk and honey and taken every morning for a few months or as prescribed by an ayurvedic practitioner.[1] Shankpushpi is also often given as tonics for brain development in children.
Shankhpushpi is renowned as a brain tonic. Ayurveda counts shankhpushpi among the group of herbal remedies known as "medhya rasayana." These remedies help boost cognition or the ability to learn and have drawn interest due to the absence of major adverse side effects associated with mainstream.

3.JYOTISHMATI (CELATRUS PANNICULATUS):

Celastrus paniculatus Willd. (Family: Celastraceae), commonly known as Malkangni (in Hindi) or Jyotishmati (in Sanskrit), was in use from time immemorial to treat brain-related disorders. C. paniculatus seeds and seed oil have been used in Ayurvedic medicine for stimulating intellect and sharpening the memory. Celastrus oil therapy in mentally-retarded children results in improvement in their I.Q. Celastrus seeds have been reported to possess hypolipidemic, antiatherosclerotic, antispermatogenic , antioxidant , anxiolytic, antistress, and nootropic activities. The seed oil contains a number of fatty acids such as oleic, linoleic, linolenic, palmitic, stearic, benzoic, and acetic acid as volatile acids and their glycerol esters mainly α, α' dipalmitoyl glycerol. The seeds also contain sesquiterpene alkaloids viz. celapanin, celapanigin, celapagin, and malkangunine. The seed oil of Jyotishmati is used as brain tonic due to its beneficial effect on memory and intellect. The phytochemicals present in Celastrus paniculatus are sesquiterpenes, alkaloids celastrine, celapanine, celapanigine, celapagine, polyalcohol (malangunin, malkanginnol, malkanguniol and paniculatusdiol). It contains triterpenoid pristimerin and sterols (β-amyrin and β-sitosterol), sesquiterpeniod polyol esters have also been isolated from Celastrus paniculatus.

4. HYPERICUM PERFORATUM (ST. JOHN'S)

St. John's wort derives from a yellow flower that people have used in herbal medicine for centuries. Some studies show that St. John's wort can treat depression, but the results of these studies are inconsistent. Researchers do not know if St. John's wort is an effective long-term treatment. Some research suggests that St. John's wort may change how the brain processes serotonin, dopamine, and norepinephrine in a similar way to some antidepressants. In some studies, St. John's wort works better than a placebo and can work just as well as tricyclic antidepressants. A 2011 review of previous research studies found that St. John's wort improved symptoms of depression in ten of the studies. However, little data suggested that it works well to treat severe depression, or that it can be a long-term depression treatment. The treatment of non-selected depressed patients with a hydro-alcoholic extract of Hypericum perforatum has been reported to have an efficacy similar to that of classical antidepressants. The effects of H. perforatum on three animal depression models have been studied: (a) an acute form of escape deficit (ED) induced by unavoidable stress; (b) a chronic model of ED, which can be maintained by the administration of mild stressors on alternate days; (c) a model of anhedonia based on the finding that repeated stressors prevent the development of appetitive behavior induced by vanilla sugar in satiated rats fed ad libitum. H. perforatum: (i) acutely protects animals from the sequelae of unavoidable stress; (ii) reverts the chronic escape deficit state maintained by repeated stressors and (iii) preserves the animal's capacity to acquire motivated appetitive behavior. Exposure to chronic stress not only induces escape deficit, but also decreases extraneuronal levels of dopamine in the nucleus accumbens shell; both behavioral and neurochemical effects are reverted by long-term treatment with antidepressants. Three-week treatment with H. perforatum reverted the chronic stress effect on extraneuronal dopamine in the nucleus accumbens. A consistent body of data in the literature suggests that, among the components of H. perforatum extract, hyperforin is the compound (or one of the compounds) responsible for the antidepressant activity. We compared the efficacy of the total extract with the efficacy of hyperforin after p.o. administration. In the acute-escape deficit model, hyperforin showed a potency of about ten times that of the total extract in protecting rats from the sequelae of unavoidable stress. Thus, hyperforin appears to be the most likely active component responsible for the antidepressant activity of H. perforatum.

5.TULSI (OCIMUM SANCTUM)

According to the journel of ayurveda and integrative medicine tulsi has antidepressant and antianxiety properties as compared to other antidepressant drugs.

Modern lifestyle has full of mental stress in all age group in human beings due to physical chemical and psychological stress. The psychotherapeutic properties of tulsi have been observed in various experimental animals. Tulsi has anti-depressant, anti-anxiety properties which can be compared to antidepressant drugs like Diazepam.

In human studies it has been observed to reduce depression, anxiety and stress and protects against aging induced memory loss/deficit. In other animals, it reportedly enhances memory and cognitive activities.

6. ASHWANGANDHA (WITHANIA SOMNIFERA)

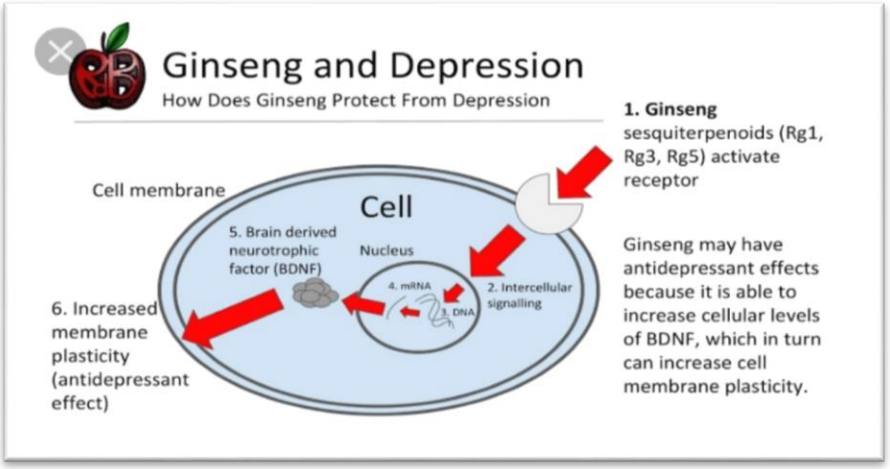
Ashwaghandha probably has more negative side effects than positive ones but it is difficult to say this with surety. Research, of course, has not involved humans but extrapolations have been made from tests on animals. These results and other determinations indicate that your diagnosis and medical history of taking antidepressants should make you cautious. These “medicines" are risky for anyone with a mood disorder. Taking supplements or herbs, in general, is a gamble and its effects on a person should be watched closely. Ashwaghandha is also known to have many effects on a variety of organs. Problems such as liver or kidney disease, cardiology issues, brain disorders, diabetes, autoimmune diseases should be red flagged for the use of this supplement.

7.GINSENG (PANAX):

Ginseng effectively suppresses stress,which is a major cause of depression. This activity has been demonstrated in depression tests using animals models. Ginseng demonstrated similar levels of efficacy as the commercially available antidepressrant.

The molecular and cellular mechanisms of Panax ginseng and its herbal formulae include modulating monoamine neurotransmitter system, upregulating the expression of neurotrophic factors, regulating the function of HPA axis, and anti-inflammatory action. This supplement comes from the gnarled root of the American or Asian ginseng plant. Siberian, Asian, and Eleuthero ginseng are different plants with different active ingredients. Practitioners of Chinese medicine have used ginseng for thousands of years to help people improve mental clarity and energy and reduce the effects of stress. Some people associate these properties of ginseng with potential solutions for the low energy and motivation that can occur with depression. However, the National Center for Complementary and Integrative Health (NCCIH) advise that none of the many studies that people have conducted on ginseng have been of sufficient quality to form health recommendations.

Mechanism of action



8. LAVENDER (LAVANDULA):

Anxiety and depression are common in dementia including in Alzheimer's disease. It is demonstrated that inhalation of dried flower heads lavender essential oil vapours improved scopolamine-induced spatial memory impairment and exhibited anxiolytic and antidepressant-like effects in scopolamine-treated rats (Hritcu et al. 2012). It is reported that the main constituents of lavender oil are linalool, linalyl acetate, cineole, terpinen-4-ol and camphor (Hritcu et al. 2012). These constituents can vary significantly in different parts of plant such as flower, leaves, stem and branches. The pure oil is most often used in aromatherapy and massage. Despite its popularity and long tradition of use, only recently scientifically based investigations into the biological activity of the various Lavandula products (essential oils or kind of extracts) have been undertaken to a greater extent. The biological actions of many of the chemical compounds found in lavender are not well understood (Hritcu et al. 2012). Therefore, the present study for the first time investigates the effect of L. officinalis aerial parts hydro-alcoholic extract on anxiety- and depression-like behaviour in scopolamine-treated rats. People anecdotally talk about the benefits of lavender, including its relaxing properties, and how it helps them get a good night's sleep. As many people with depression also experience anxiety and sleep issues, lavender could help them sleep without the side effects of sleeping pills. According to a 2012 systematic review inhaling lavender aromas before sleeping, did help people get to sleep. However, the studies were small, and most had methodological issues, so researchers need to do more studies to support the findings. However, a 2015 randomized controlled trial does provide more evidence that lavender may help with sleep. In that study, two groups practiced healthy sleep hygiene, with one group wearing a lavender aromatherapy patch. Both groups were sleeping better, but the results were stronger in the lavender group. Lavender oil is a popular essential oil. People typically use lavender oil for relaxation and reducing anxiety and mood disturbances. A 2013 review of various studies suggested that lavender might have significant potential in reducing anxiety and improving sleep. Lavender has mixed results in studies that assess its impact on anxiety. However, its effectiveness as a treatment for ongoing depression has little high-quality evidence in support at the current time.

9. JASMINE (JASMINUM):

When you inhale the molecules from jasmine, your body receives messages from the limbic system which is responsible for influencing the nervous system. You can have jasmine in your room as a plant to relieve your anxiety and depression systems or use it as an essential oil to put in a diffuser to catch the scent. As well as anxiety and depression, jasmine can also improve your focus, help with sleeping, balance hormones, and lower your risk of infection. This shows that the jasmine plant is multi-function and can help improve your quality of life.

10.RHODIOLA (RHODIOLA ROSEA):

Rhodiola is an herb linked to a variety of potential health benefits when taken in supplement form. These include reduced depressive symptoms and an improved stress response, which can help your body adapt to stressful situations. The herb may exert antidepressant effects via its ability to enhance nerve cell communication and reduce overactivity of the hypothalamic-pituitary-adrenocortical (HPA) axis. The HPA axis is a complex system that regulates your body's stress response. Research suggests overactivity of the HPA axis may be associated with major depression. Some studies show that supplementing with rhodiola may benefit those with depression. For example, a study in 57 people with depression found that treatment with 340 mg of rhodiola extract per day for 12 weeks led to clinically meaningful reductions in depressive symptoms. What's more, while rhodiola treatment was less effective than the antidepressant medication Sertraline, it caused much fewer side effect. Another study found that a supplement composed of rhodiola and saffron significantly reduced depression and anxiety symptoms in adults with mild to moderate depression after 6 weeks.

MEDICINAL MEDICINES

1. IMIPRAMINE
2. MOCLOBEMIDE
3. CLORGYLINE
4. FLUOXESTINE
5. PAROXETINE
6. SERTRALIN
7. TRAZODONE
8. AMINEPTINE
9. DOXEPIN
10. CLOMIPRAMINE

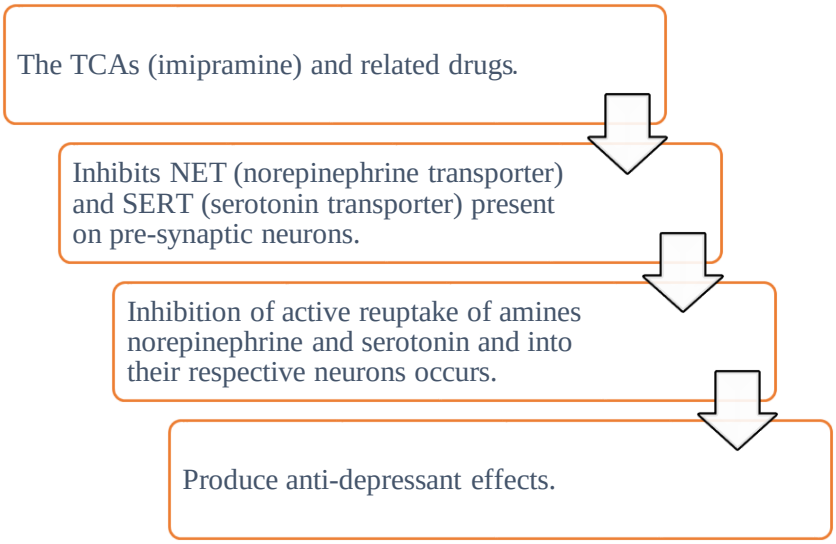
1. IMIPRAMINE

It is trycyclic anti-dipressant.

These of drug produce anti-depresant action by increasing the level of noradrenaline (NA) and serotonin by inhibiting reuptake of NA and serotonin in neurons.

Tricyclic anti-depressants produce sedation, dry mouth etc.

- **Mechanism of Action:**



- **Pharmacological actions:**

i. Central nervous system:

In depressed patients, the mood is slowly elevated and patients begin to take interest in self and surroundings, after continuous treatment of 2-3 weeks.

It lowers seizure threshold, but in case of overdose, it produces convulsions.

ii. Cardiovascular system:

It produces tachycardia and postural hypotension.

Overdose produces arrhythmias.

iii. Autonomic nervous system:

Potent anti-chalinergic effects are produced by most TCAs and produce some side effects such as dry mouth, blurred vision, constipation etc.

- **Pharmacokinetics:**

Absorption by oral route is good of TCAs.

TCAs highly bound to plasma and tissue protiens.

They are widely biotransformed in liver.

Over 1-2 weeks, metabolites are excreted in urine.

- **Adverse effects:**

Dry mouth, bad taste, constipation.

Weakness, mental confusion and sedation.

Sweating, weight gain.

Especially in older patients, postural hypotension occurs.

Sexual: Erection is delayed.

- **Interactions:**

CNS depressants such as alcohols and anti-histaminics are potentiated by TCAs.

TCAs can be displaced from protein binding sites by aspirin, phenytoin, phenyl-butazone etc. and increase its toxicity

Metabolism of TCAs is enhanced by carbamazepine and other enzyme inducers while it is inhibited by SSRIs.

Uses:

TCAs and related anti-depressants are used to relieve symptoms of depression.

TCAs particularly clomipramine, are highly efficient in obsessive-compulsive disorders.

TCAs are also used in neuropathic pain.

TCAs particularly clomipramine, delay and in some cases inhibit ejacuation.

2. MOCLOBEMIDE:

It is reversible and selective MAO-A inhibiter with short duration of action and full MOA activity is restored within 1-2 days of stopping the drug.

Its effective antidepressant, comparable to TCAs.

Its effective antidepressant, comparableto TCAs.

It lacks the anticholinergic, sedative, cognitive, psychomotor and cardiovascular adverse effects of typical TCAs and is safer in overdose.

Adverse drug reaction:

Nausea, dizziness, headache, insomnia, rarely excitement and liver damage.

Use: alternative for TCAs to moderate depression and social phobia.

Dose: 150 mg; BD or TID (max 600 mg/kg/day)

- **Pharmacokinetics of Moclobemide**

In humans moclobemide is rapidly and almost completely absorbed and totally metabolised via the liver. Peak plasma levels occur 0.3 to 2 hours after oral administration. The bioavailability increases during the first week of therapy from 60% to 80% and more. The elimination half-life is around 2 hours. It is moderately bound to plasma proteins, especially albumin. However, the short disposition half life somewhat increases after repeated dosing; moclobemide has an intermediate elimination half life for systemic clearance and an intermediate volume of distribution. Despite its short half-life the pharmacodynamic action of a single dose persists for approximately 16 hours. The drug is almost completely metabolized in the liver; it is a substrate of CYP2C19 and an inhibitor of CYP2C19, CYP2D6 and CYP1A2. Less than 1 percent of the drug is excreted unchanged; 92 percent of the metabolised drug is excreted within the first 12 hours. The main metabolites are the N-oxide Ro 12-5637 formed via morpholine N-oxidation and lactam derivative Ro 12-8095 formed via morpholine C-oxidation; active metabolites are found only in trace amounts. The unchanged drug (less than 1%) as well as the metabolites are excreted renally (in urine). The main degradation pathway of moclobemide is oxidation. About 44 percent of the drug is lost due to the first pass effect through the liver. Age and renal function do not affect the pharmacokinetics of moclobemide. However, patients with significantly reduced liver function require dose reductions due to the significant slowing of metabolism of moclobemide. Food slows the absorption but does not affect the bioavailability of moclobemide.

- **Pharmacology of Moclobemide**

It has been described as a 'slow binding inhibitor', whereby conformational changes to either moclobemide or the enzyme to MAO-A slowly form a more tightly bound complex, resulting in the non-competitive MAO inhibition by moclobemide. With three times daily dosing the inhibition on MAO-A was relatively constant with moclobemide. The MAO inhibition of moclobemide lasts about 8–10 hours and wears off completely by 24 hours after dosing. The inhibition of MAO-A by moclobemide is 10 times more potent than the irreversible MAOIs phenelzine and approximately equivalent to tranylcypromine and isocarboxazid.

Moclobemide increases levels of extracellular monoamines and decreases levels of their metabolites in rat brains; tolerance to these effects does not seem to occur with chronic use of moclobemide. Moclobemide lacks anticholinergic effects and cognitive impairments can be improved by moclobemide. Moclobemide suppresses the unstimulated release of certain proinflammatory cytokines which are believed to be involved in the pathophysiology of major depression and stimulates the release of anti-inflammatory cytokines. Long-term treatment with moclobemide leads to an increase in cyclic adenosine monophosphate (cAMP) binding to cAMP-dependent protein kinase (PKA).

Moclobemide is chemically unrelated to irreversible MAOI antidepressants and only has a very weak pressor effect of orally administered tyramine. In humans, the n-oxide metabolites of moclobemide and moclobemide itself are the compounds that produce most of the inhibition of MAO-A; other metabolites are significantly less potent than the parent compound.

In healthy people moclobemide has a relatively small suppressing effect on REM sleep; in contrast, depressed people who have been treated with moclobemide, progressively show improved sleep over a 4-week period, with an increase in stage 2 non-rapid eye movement (NREM) sleep and rapid eye movement (REM) sleep. There have been conflicting findings with regard to moclobemide altering cortisol levels and whether moclobemide increases growth hormone levels. Testosterone levels increase significantly with long-term use of moclobemide in depressed males.

Moclobemide also has neuroprotective properties in its demonstrated anti-hypoxia or anti-ischemia effects; there is a possibility that moclobemide may possess similar neuro-rescuing properties, similar to selegiline, however, research is required to determine this.[8] Moclobemide has also been demonstrated in a single dose research study to possess antinociceptive properties.

3. PAROXETINE (PAXIL)

Indicated for Social Phobia, plus five others.

Significantly more anti-ACH affinity, thus more anti-ACH side effects.

• Intermediate half-life, no active metabolites. Potential for drug-drug interactions, especially psychiatric (2D6) is of concern.

• Worst side effect profile and highest rates of sexual dysfunction. May be d.o.c. for premature ejaculation. Liquid preparation available (orange).

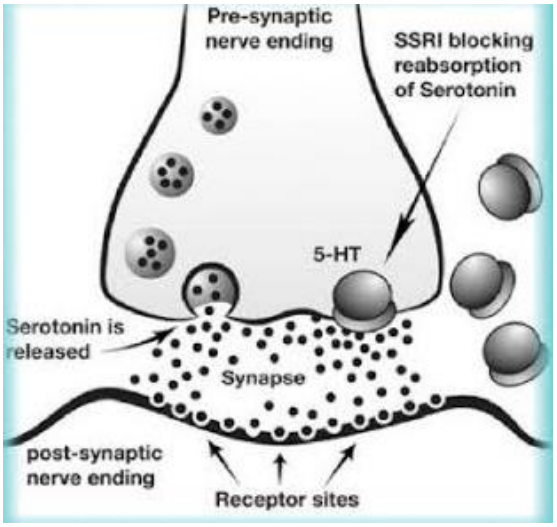
At higher doses, may be the most cost effective.

Available in sustained release form.

- **Mechanism of action.**

It is thought at SSRIS work on easing depression by blocking the reuptake of serotonin at the synapse.

This allows more serotonin to remain in the synaptic cleft where it can then bind/ activate receptors How Paxil Works



4. TRAZODONE

- **Mechanism of action**

The drug is thought to act primarily as an antagonist at 5-HT2-A and 5 HT2-C presynaptic receptors, so increasing serotonin release.

- **Adverse effects:**

Drowsiness (up to 40%, likely related to blockade of 5-HT2 A, alpha-1 and H1 receptors).
Postural hypotension
Xerostomia (up to 30%)
Priapism, sexual dysfunctions.

- **Therapeutic uses:**

Depression (as a second choice drug, mainly in patients with agitation and insomnia).
As an unlabeled hypnotic, since it is not associated with tolerance or dependence.

- **Pharmacology of Trazodone:**

Trazodone is a mixed agonist and antagonist of various serotonin receptors, antagonist of adrenergic receptors, weak histamine H1 receptor antagonist, and weak serotonin reuptake inhibitor. More specifically, it is an antagonist of 5-HT2A and 5-HT2B receptors, a partial agonist of the 5-HT1A receptor, and an antagonist of the α1- and α2-adrenergic receptors. It is also a ligand of the 5-HT2C receptor with lower affinity than for the 5-HT2A receptor. However, it is unknown whether trazodone acts as a full agonist, partial agonist, or antagonist of the 5-HT2C receptor. Trazodone is a 5-HT1A receptor partial agonist similarly to buspirone and tandospirone but with comparatively greater intrinsic activity. A range of weak affinities (Ki) have been reported for trazodone at the human histamine H1 receptor, including 220 nM, 350 nM, 500 nM, and 1,100 nM.

Trazodone has a minor active metabolite known as meta-chlorophenylpiperazine (mCPP), and this metabolite may contribute to some degree to the pharmacological properties of trazodone. In contrast to trazodone, mCPP is an agonist of various serotonin receptors. It has relatively low affinity for α1-adrenergic receptors unlike trazodone, but does high affinity for α2-adrenergic receptors and weak affinity for the H1 receptor. In addition to direct interactions with serotonin receptors, mCPP is a serotonin releasing agent similarly to agents like fenfluramine and MDMA. In contrast to these serotonin releasing agents however, mCPP does not appear to cause long-term serotonin depletion (a property thought to be related to serotonergic neurotoxicity).

Trazodone's 5-HT2A receptor antagonism and weak serotonin reuptake inhibition form the basis of its common label as an antidepressant of the serotonin antagonist and reuptake inhibitor (SARI) type.
Trazodone is well-absorbed after oral administration. Its bioavailability is 65 to 80%. Peak blood levels of trazodone occur 1 to 2 hours after ingestion and peak levels of the metabolite mCPP occur after 2 to 4 hours. Absorption is somewhat delayed and enhanced by food.[citation needed]

Trazodone is not sequestered into any tissue. The medication is 89 to 95% protein-bound. The volume of distribution of trazodone is 0.8 to 1.5 L/kg. Trazodone is highly lipophilic.

The metabolic pathways involved in the metabolism are not well-characterized. In any case, the cytochrome P450 enzymes CYP3A4, CYP2D6, and CYP1A2 may all be involved to varying extents. Trazodone is known to be extensively metabolized by the liver via hydroxylation, N-oxidation, and N-dealkylation. Several metabolites of trazodone have been identified, including a dihydrodiol metabolite (via hydroxylation), a metabolite hydroxylated at the para position of the meta-chlorophenyl ring (via CYP2D6), oxotriazolepyridinepropionic acid (TPA) and mCPP (both via N-dealkylation of the piperazinyl nitrogen mediated by CYP3A4), and a metabolite formed by N-oxidation of the piperazinyl nitrogen. CYP1A2, CYP2D6, and CYP3A4 genotypes all do not seem to predict concentrations of trazodone or mCPP. In any case, there are large interindividual variations in the metabolism of trazodone. In addition, poor metabolizers of dextromethorphan, a CYP2D6 substrate, eliminate mCPP more slowly and have higher concentrations of mCPP than do extensive metabolizers.

mCPP is formed from trazodone by CYP3A4 and is metabolized via hydroxylation by CYP2D6 (to a para-hydroxylated metabolite). It may contribute to the pharmacological actions of trazodone. mCPP levels are only 10% of those of trazodone during therapy with trazodone, but is nonetheless present at concentrations known to produce psychic and physical effects in humans when mCPP has been administered alone. In any case, the actions of trazodone, such as its serotonin antagonism, might partially overwhelm those of mCPP. As a consequence of the production of mCPP as a metabolite, patients administered trazodone may test positive on EMIT II urine tests for the presence of MDMA ("ecstasy").

5. SERTRALINE:

- **Mechanism of Action**

Sertraline is an inhibitor of the SERT transporter, this is linked to its mechanism of action as antidepressant. It has mild effects as dopamine transporter inhibitor, but this hasn’t been proven to have a clear clinical implication. Some clinicians attribute sertraline an activating effect, which could probably be linked to this mild dopaminergic effect. Also, sertraline has affinity for sigma 1 receptors. The clinical relevance of this is still unknown.

- **Clinical Uses:**

sertraline6Sertraline was approved in the US for the treatment of major depression. It is also approved for use in panic disorder, premenstrual dysphoric disorder, posttraumatic stress disorder, obsessive compulsive disorder. In 2003, sertraline was approved for social anxiety disorder.

- **Pharmacokinetics:**

sertraline9The elimination half life of sertraline is around one day: 26 to 32 hours. Regarding CYP450 isoenzymes, sertraline is modest inhibitor of CYP2D6. As we discuss in other presentations, this opens the theoretical possibility to potential drug interactions with tricyclic antidepressants and antiarrhythmics.

- **Medicinal uses**

Depression

Multiple controlled clinical trials established efficacy of sertraline for the treatment of depression. Sertraline is also an effective antidepressant in the routine clinical practice. Continued treatment with sertraline prevents both a relapse of the current depressive episode and future episodes (recurrence of depression).

In several double-blind studies, sertraline was consistently more effective than placebo for dysthymia, a more chronic variety of depression, and comparable to imipramine in that respect. Sertraline also improves the depression of dysthymic patients to a greater degree than psychotherapy.

Sertraline provides no benefit to children and adolescents with depression.

- **Comparison with other antidepressants**

In general, sertraline efficacy is similar to that of other antidepressants. For example, a meta-analysis of 12 new-generation antidepressants showed that sertraline and escitalopram are the best in terms of efficacy and acceptability in the acute-phase treatment of adults with depression. Comparative clinical trials demonstrated that sertraline is similar in efficacy against depression to moclobemide, nefazodone, escitalopram, bupropion, citalopram, fluvoxamine, paroxetine, venlafaxine and mirtazapine. Sertraline may be more efficacious for the treatment of depression in the acute phase (first 4 weeks) than fluoxetine.

There are differences between sertraline and some other antidepressants in their efficacy in the treatment of different subtypes of depression and in their adverse effects. For severe depression, sertraline is as good as clomipramine but is better tolerated. Sertraline appears to work better in melancholic depression than fluoxetine, paroxetine, and mianserin and is similar to the tricyclic antidepressants such as amitriptyline and clomipramine. In the treatment of depression accompanied by OCD, sertraline performs significantly better than desipramine on the measures of both OCD and depression. Sertraline is equivalent to imipramine for the treatment of depression with co-morbid panic disorder, but it is better tolerated. Compared with amitriptyline, sertraline affords a greater overall improvement in quality of life of depressed patients.

- **Depression in elderly**

Sertraline used for the treatment of depression in elderly (older than 60) patients is superior to placebo and comparable to another SSRI fluoxetine, and tricyclic antidepressants (TCAs) amitriptyline, nortriptyline and imipramine. Sertraline has much lower rates of adverse effects than these TCAs, with the exception of nausea, which occurs more frequently with sertraline. In addition, sertraline appears to be more effective than fluoxetine or nortriptyline in the older-than-70 subgroup. Accordingly, a meta-analysis of antidepressants in older adults found that sertraline, paroxetine and duloxetine were better than placebo. On the other hand, in a 2003 trial the effect size was modest, and there was no improvement in quality of life as compared to placebo. With depression in dementia, there is no benefit of sertraline treatment compared to either placebo or mirtazapine.

- **Pharmacology of sertraline:**

Sertraline is a selective serotonin reuptake inhibitor (SSRI). By binding serotonin transporter (SERT) it inhibits neuronal reuptake of serotonin and potentiates serotonergic activity in the central nervous system. It does not significantly affect norepinephrine transporter (NET), serotonin, dopamine, adrenergic, histamine, acetylcholine, GABA or benzodiazepine receptors.

Sertraline also shows relatively high activity as an inhibitor of the dopamine transporter (DAT) and antagonist of the sigma σ1 receptor (but not the σ2 receptor). However, sertraline affinity for its main target (SERT) is much greater than its affinity for σ1 receptor and DAT. Although there could be a role for the σ1 receptor in the

pharmacology of sertraline, the significance of this receptor in its actions is unclear. Similarly, the clinical relevance of sertraline's blockade of the dopamine transporter is uncertain.

6. CLOMIPRAMINE:

- **Pharmacology of clomipramine:**

The antidepressant effects of clomipramine are thought to be due to reuptake inhibition of serotonin and norepinephrine, while serotonin reuptake inhibition only is thought to be responsible for the effectiveness of clomipramine in the treatment of OCD. Conversely, antagonism of the H1, α1-adrenergic, and muscarinic acetylcholine receptors is thought to contribute to its side effects. Blockade of the H1 receptor is specifically responsible for the antihistamine effects of clomipramine and side effects like sedation and somnolence (sleepiness). Antagonism of the α1-adrenergic receptor is thought to cause orthostatic hypotension and dizziness. Inhibition of muscarinic acetylcholine receptors is responsible for the anticholinergic side effects of clomipramine like dry mouth, constipation, urinary retention, blurred vision, and cognitive/memory impairment. In overdose, sodium channel blockade in the brain is believed to cause the coma and seizures associated with TCAs while blockade of sodium channels in the heart is considered to cause cardiac arrhythmias, cardiac arrest, and death. On the other hand, sodium channel blockade is also thought to contribute to the analgesic effects of TCAs, for instance in the treatment of neuropathic pain.

The exceptionally strong serotonin reuptake inhibition of clomipramine likely precludes the possibility of its antagonism of serotonin receptors (which it binds to with more than 100-fold lower affinity than the SERT) resulting in a net decrease in signaling by these receptors. In accordance, while serotonin receptor antagonists like cyproheptadine and chlorpromazine are effective as antidotes against serotonin syndrome, clomipramine is nonetheless capable of inducing this syndrome. In fact, while all TCAs are SRIs and serotonin receptor antagonists to varying extents, the only TCAs that are associated with serotonin syndrome are clomipramine and to a lesser extent its dechlorinated analogue imipramine, which are the two most potent SRIs of the TCAs (and in relation to this have the highest ratios of serotonin reuptake inhibition to serotonin receptor antagonism). As such, whereas other TCAs can be combined with monoamine oxidase inhibitors (with caution due to the risk of hypertensive crisis from NET inhibition; sometimes done in treatment-resistant depressives), clomipramine cannot be due to the risk of serotonin syndrome and death. Unlike the case of its serotonin receptor antagonism, orthostatic hypotension is a common side effect of clomipramine, suggesting that its blockade of the α1-adrenergic receptor is strong enough to overcome the stimulatory effects on the α1-adrenergic receptor of its NET inhibition.

- **Clinical uses of clomipramine:**

1. Obsessive–compulsive disorder (OCD) which is its only U.S. FDA-labeled indication. Other regulatory agencies (such as the TGA of Australia and the MHRA of the UK) have also approved clomipramine for this indication.
2. Major depressive disorder (MDD) a popular off-label use in the US. It is approved by the Australian TGA and the United Kingdom MHRA for this indication. Some have suggested the possible superior efficacy of clomipramine compared to other antidepressants in the treatment of MDD, although at the current time the evidence is insufficient to adequately substantiate this claim.
3. Panic disorder with or without agoraphobia.
4. Body dysmorphic disorde
5. Cataplexy associated with narcolepsy. Which is a TGA and MHRA-labeled indication for clomipramine.
6. Premature ejaculation
7. Depersonalization disorder
8. Chronic pain with or without organic disease, particularly headache of the tension type.

9. Sleep paralysis, with or without narcolepsy

ADVANTAGE OF HERBAL ANTIDEPRESSENT OVER MODERN MEDICINE

When compared with the modern medicine, you'll see that the traditional medicine has a lot of benefits that you probably never knew about. They are all the same in different countries of the world like United States, Nigeria, Ghana, India, Pakistan and others.
Some of them include:

- **Low cost**

Traditional medicines tend to sell at lower prices when compared with the modern medicines, this is probably because of the low cost of research, testing, marketing and other production processes. If you visit a qualified naturopath, he or she will prescribe and administer a medication that you probably would have gotten at a costlier price if it were to be in a pharmacy. Another reason the for the low cost of the traditional medicines is that they are usually sold by the manufacturers, thereby eliminating the roles of the retailers and wholesalers that would want to make their own profit.

- **Availability**

You can grow simple herbs like chamomile and peppermint in your home garden, making it more available than the modern medicines that must be gotten in a pharmacy. They are also administered without prescription; however, this varies with the type of ailment you are suffering from. Also, in some countries of the world, medicinal herbs may be the only treatment available to the majority of people for some specific ailments.

Reduced Risk of Side Effects and Safety

Herbal advocates claim there are fewer unintended consequences with herbs than with pharmaceutical drugs, but there is no trial evidence to support these claims. Advertisements and the accompanying literature for prescription drugs typically have a long list of possible side-effects, but without study, side effects remain largely undocumented and/or unknown. Some herbs do come with warnings, such as not to take if you're pregnant or lactating. Another argument in favour of herbal medicines is the safety factor versus long-term effects of non-herbal drugs. Again, this may be true in a personal experience, but there is little to no scientific evidence so far to back up such claims.

Effective for complicated and chronic conditions

Another great advantage of herbal drugs is that they tend be more reliable and effective for complicated and resistant health complications. In some cases, like arthritis, were drugs like Vioxx that was used for its treatment was recalled because of its risk of increasing cardiovascular complications, herbal medicines tend to become the next option.
Alternative arthritis treatments like change in diets which may include addition of simple herbs, elimination of vegetables and reduction in the consumption of white sugar are some ways of treating arthritis.

Review of Ayurvedic Herbal Medications

In another review of studies, the researchers examined Ayurvedic medication for the treatment of schizophrenia and concluded, "Ayurvedic medication may have some effects for treatment of schizophrenia.

Herbs Are Food

The argument that herbs are safe by virtue of being a food is not necessarily valid. Herbs are touted as safe simply because they are foods. Most people find this to be true in their personal uses of herbs. However, it should be noted that individuals can be allergic to herbs just as they are to any other food or not use them in proper dosage, causing problems.

DISADVANTAGE OF HERBAL ANTIDEPRESSENT OVER THE MODERN MEDICINE

Like we all know and always say, herbal medicines also have its advantages and are not appropriate for all health conditions. Some of the disadvantages of herbal medicines include:

- **Lack of dosage instructions**

Every drug should have a prescription in order to avoid over-dosing. However, in Nigeria, what we mostly see it take one spoon daily of which many people don't keep to. Another issue is when people grow and prepare this herbs themselves, they tend to take them without being careful of the best dosages and proportions thereby leading to accidental overdosing.

- **Risk of using inferior herb:**

Another great disadvantage of using herbs is the risk of purchasing adulterated products. This is very popular in under-developed countries or countries with high rate of poverty. Although you might see also see this in the case of modern drugs, the case is reduced because companies tend to provide means of verifying your drugs in the pharmacies before paying for them. Many modern drugs that are being manufactured now come with different methods of authenticating the originality of the drugs. One of the methods is by sending an SMS of a pin that can be gotten by scratching the packet of a drug to38351 (Pharma secure), 38353 (Sproxil), 1393 (Goldkeys), 20966 (UBQ) etc., the number varies with the service the drug manufacturers chose to work with and you'll always see it in the drug packet. After a few minutes of sending the SMS, you'll receive a reply showing the name of the drug and whether its fake or genuine.

- **Medication interactions**

Many people warn against combining the use of herbal drugs with modern ones. This is because traditional drugs can interact with different medications. This is the major reason most herbal drugs come with warnings prompting people to use them with caution. To avoid this, it becomes necessary for everyone to discourse his or her herbal supplements with experienced medical personnel to avoid complications and dangerous interactions.

- **Not appropriate for all conditions**

Drugs from the pharmaceuticals tend to treat serious and complicated ailments more effectively than other alternatives. An herbalist can't be performing a surgery on an individual or run modern diagnostic tests. Also, he can't be able to stop a heart attack heal an appendicitis faster better than a conventional doctor that would use modern equipment and facilities.

- **Wild herbs are usually associated with poison risks**

Going to the forest to harvest herbs is usually risk and you need to take proper measures in order to survive some wild animals and other things. Also, you might enter the forest only to encounter weeds that look like the herbs thereby posing a risk of you picking the wrong plants or the wrong parts of the right plants.

- **Are Herbal Medicines Good for Me?**

Just like every other drug, they are good but should be taken with caution. Be careful if you are the person to pick the herbs to avoid picking the wrong ones as many weeds tend to contain poisons. You need to take the following tips in order to get the best of every drug.

ADVANTAGE OF MODERN MEDICINE OVER THE HERBAL ANTIDEPRESSENT

Modern medicine is also known as Western medicine, and is considered to be much more effective than traditional herbal and homeopathic treatments.

Advances in trauma treatment through modern medicine have life-saving implications. Through adequate training and practice, surgeons and nurses work together in emergency situations treating severe injuries caused by accidents such as automobile crashes or natural disasters.

Modern medicine treats symptoms in addition to the presenting illness in order to alleviate patient discomfort and speed the healing process. With symptoms under control, patients can resume daily activities while the illness is treated.

Advances in medical technology and tools allow doctors to quickly and precisely identify patient issues. For example, X-ray machines diagnose broken bones and determine that a cast is the appropriate treatment to allow the injury to heal.

Flexibility in modern medicine provides patients with the ability to make inquiries about their symptoms and possible diagnosis online. Depending on the illness, many patients receive treatment at home or on an outpatient basis, which reduces expenses.

DISADVANTAGES OF MODERN MEDICINES OVER THE HERBAL ANTIDEPRESSENT:

1. It's More Focused on Treating the Sick Than Dealing With Maintaining Health.

Modern medicine primarily uses surgery, radiation, and drugs to facilitate improvements in health and in the treatment of various illnesses. It is primarily involved in the treatment of the sick, unlike alternative therapies, which also deal with the maintenance of health.

Why This Is Bad for the Patient

- In some cases, the therapy offered by conventional medicine is symptomatic management instead of addressing the cause of the illness.
- Symptomatic management can result in the progression of the disease as necessary lifestyle changes or corrective treatment is not initiated.
- The culture becomes more focused on cures than on prevention. This can have a negative psychological effect wherein the population live unhealthy lives due to inattention to how they can help themselves on a daily basis.
- Prevention saves the individual and country money in the long-term, whereas a cure-obsessed culture ends up costing everyone more money.

2. It's Responsible for Many Deaths in America Annually.

There are statistics available suggesting that modern medicine is responsible for many deaths in America annually. The trend in modern medicine has been towards alienating all "competition" from alternative medicine. This has led to a number of negative consequences.

Why This Is Bad for the Patient

- Hospitals get sued, driving up prices.
- 750,000 deaths occur in the United States as a direct result of poor medical care.
- It's estimated that nine million Americans are unnecessarily hospitalized every year.
- Fear of the hospital creates stress in patients.
- More people avoid getting the help they need, instead opting for easy solutions that might cause worse problems in the future.
- 20 million unnecessary prescriptions are written for antibiotics to treat minor VIRAL infections each year.

3. It Squashes Competition From Alternative Medicine.

There are claims made by modern medicine that alternative therapies are not scientific. To some extent, it is true that the benefits of natural medicine sometimes elude scientific study. The methods used by practitioners of natural medicine may not all be medically proven, but they are effective in some instances.

Most of the risks associated with natural medicine are insignificant compared to those associated with conventional medicine. However, it is important that practitioners of natural medicine recognize when conventional medicine is more appropriate. When alternative medicine cannot appropriately address an injury or illness, it is necessary for the alternative medicine practitioner to refer patients onwards to conventional medicine.

Most people are aware of the overuse and perils of modern medicine, but they also know that it can sometimes treat illnesses very effectively. It's important to have a choice between modern medicine and natural medicine, because each has a place in the management of disease and the maintenance of health.

Why This Is Bad for the Patient

- Business growth declines, limiting jobs in the alternative sector.
- New inventions don't come into being.
- Alternative solutions are not taken seriously.
- Patients become obsessed with cures, rather than taking affordable, preventative measures to maintain their health.

4. Drugs All Have Side-Effects.

The use of pharmaceutical drugs in modern medicine comes with all sorts of unintended consequences. These drugs can cause many side-effects to emerge that can negatively affect one's health. In the U.S.A., pharmaceutical companies have too much control over medicine. Sometimes, doctors are encouraged to prescribe certain medications for the financial gain of these drug companies.

Why This Is Bad for the Patient

- Sometimes, getting treated with pharmaceuticals leads to side-effects that cause more harm than good, causing the individual to spend even more money.
- Lawsuits end up costing patients, companies, and hospitals billions every year, driving up costs for everyone else.
- Overprescription of opioids has devastated entire communities around the globe.

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