

A REVIEW ON HORRENDOUS DEPRESSION AND ITS AMENDATORY DRUG

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ABSTRACT

Depression (major depressive disorder) is a common and serious medical illness that negatively affects the health of the person. It can lead to a variety of emotional and physical problems that decrease the ability to function properly. Depression is the most widely recognized mental problem detailed in each next individual in today's way of life. It has turned into the third driving reason for worldwide sickness trouble, and is representing 4.3% of all out inability changed life years. Assuming these proceeds for long, it will end up being the main source of infection trouble by the year 2030. The Bupropion was first and foremost found to treat the Major Depressive Disorder (MDD) and is often utilized for smoking-suspension. Bupropion is the much requested medication among the adolescent. As a rule, youth going through the period of depression might see an improvement in different indications like superior mind-set, further developed focus, more energy and better rest in the wake of taking this drug.

KEYWORDS:

Depression, Smoking-suspension, Bupropion, Antidepressants

INTRODUCTION:

Major Depressive Disorder (MDD) is a significant general wellbeing worry with huge weakness in mental, word related, and social working. The commonness rates for depression are assessed to be around 3.2% in patients without comorbid actual sicknesses and 9.3% to 23.0% in patients with chronic conditions. It is the fourth cause of disability around the world and is estimated to be the second leading cause of disability by 2020^[1].

Selective serotonin reuptake inhibitors (SSRIs) are the appropriate first-line options for the treatment of depression along with psychotherapeutic interventions, but many patients either do not respond to different options or intolerant to the undesired effects of medications^[2].

Despite multiple treatment regimen, about 60% of patients with MDD continue to report residual impairments even after treatment^[3]. Certain people have myth related to depression as they still believe that it is because of some weakness in personality, or one can cure by oneself, or that medication would go lifelong and are mere sedatives^[4]. Normally the patients of depression introduce themselves to therapist with the objections of restoratively unexplained physical manifestations, or masked melancholy. Depression has turned into the third driving reason for worldwide infection trouble, and is representing 4.3% of aggregate handicap changed life years. Depression is the

most common and treatable problem or disorder but can continue for lifetime if not treated properly. . It affects the mental and emotional wellbeing and ultimately affects the overall quality of life ^[5].

Depression, a staggering state for the adults:

Studies in the elderly recommend that, particularly passing in the family and monetary issues are the most destroying events for depression and the equivalent occurs in the situation of youths. Especially elderly females are in the capture of this dreadful psychic disorder ^[6]. The casual attribution of an individual is responsible for the nature of depression which is followed by the uncontrollable events ^[7]. According to a community survey the prevalence rate of depression amongst the adolescents is between 1.8%-7.8% ^[8]. From the past most twenty years, depression has been experienced as a significant mental medical issue.

According to the research done for psychiatric morbidity amongst the school adolescents, it was found that 29% of girls & 23% of boys suffering from depression were having this common disorder ^[9]. The fig. 1 given below, explains the percentage of suicidal case amongst school going adolescents ^[10].

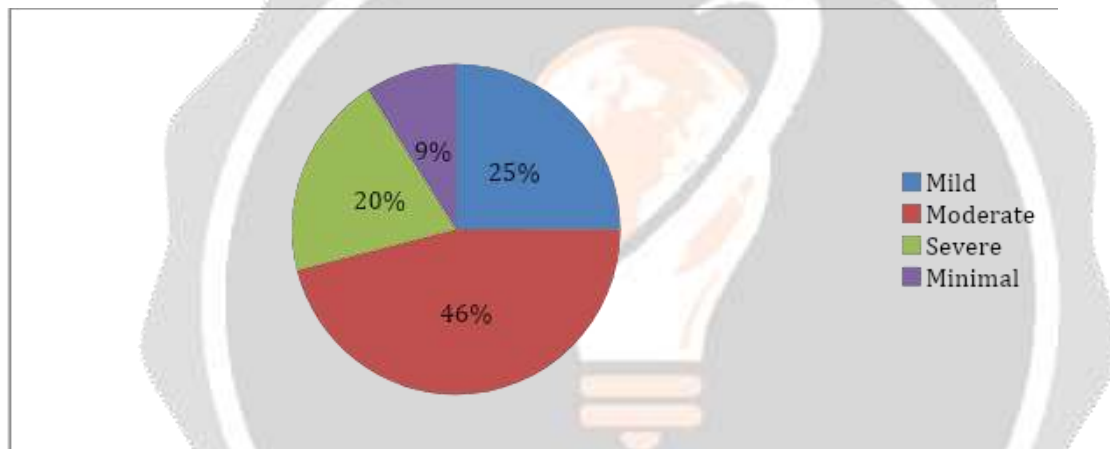


Fig. 1: Percentage of depression amongst school going adolescents.

An older juvenile (15-17yrs.) have 1.5-times more prominent hazard of depression when contrasted with more youthful juvenile (12-14yrs.). Parental mental health is also an important concern regarding the chances of occurrence of depression ^[11]. Another version of BDI which is used for measuring the depression in younger age group is known as Children's Depression Inventory (CDI) ^[12]. Suicide has become the third driving reason for death among youths and youthful grown-ups. Below figure is the representation of suicidal rates amongst male and female of different ages, (Fig. 2) ^[13].

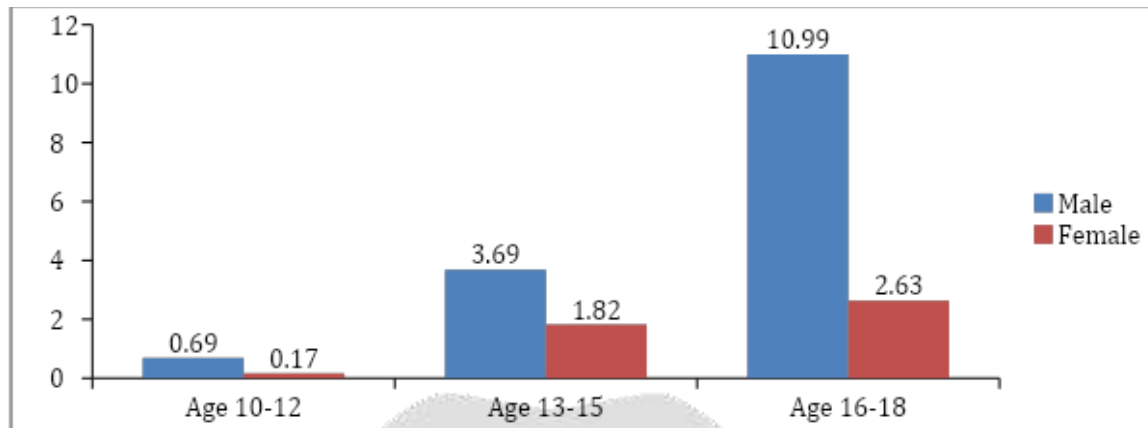


Fig. 2: Representation of suicidal rates in India by age ranging (10-18) & gender.

FACTORS RESPONSIBLE FOR DEPRESSION:

Attribution style is the major contributing factor responsible for making the person vulnerable to depression. It is responsible for maintaining the depressive symptoms once they develop^[14]. The various factors that contribute to depression include^[15]:

- Genetic characteristics
- Changes in hormones level
- Certain medical illness
- Substance abuse

TYPES OF DEPRESSION:

MAJOR DEPRESSION: A mood disorder in which there are feelings of sadness, loss and anger with everyday life.

DYSTHYMIA: Dysthymia is a chronic type of depression disorder in which a person's mood is regularly low.

SEASONAL AFFECTIVE DISORDER: A depressive mood disorder that occurs and disappears at roughly the same time each year.

DEPRESSIVE PSYCHOSIS: It is a combination of a depressed mood along with psychosis or a loss of touch with reality.

POSTPARTUM DEPRESSION: Short term depression experienced by women after giving birth. Hormonal changes after childbirth can cause Postpartum depression.

PREMENSTRUAL DYSPHORIC DISORDER: Extreme mood shifts may start to occur in women beginning 7 to 10 days before their period starts and may continue into the first few days of the period.

TYPES OF ANTIDEPRESSANTS:

Antidepressants are the medications that can help relieve symptoms of depression, social anxiety disorder, anxiety disorders, seasonal affective disorder and dysthymia, or mild chronic depression as well as other conditions.

Varieties of antidepressants are available in the market, but selection of particular antidepressant according to the particular condition of the patient is very essential to get rid of it ^[16]. Given below figure is the representation of the various types of antidepressants according to their generation, (Figure 3) ^{[17], [18]}.

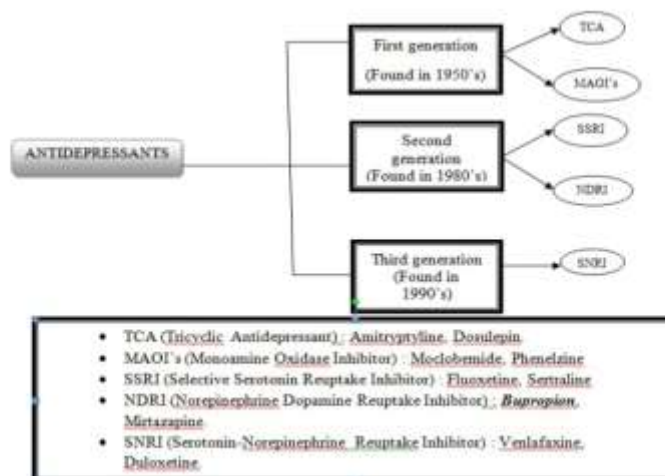


Fig 3: Flow chart with examples for various types of antidepressant

BUPROPION:

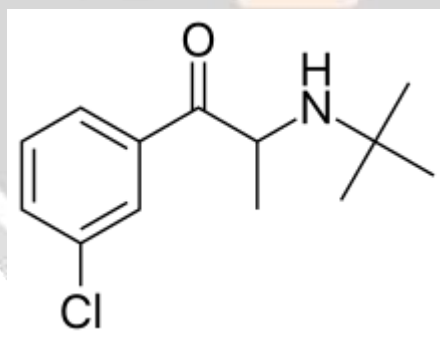


Fig 4: Structure of Bupropion

Bupropion was invented by Nariman Mehta of Burroughs Wellcome (now GlaxoSmithKline) in 1969, and the US patent for it was granted in 1974. It was approved by the U.S. Food and Drug Administration (FDA) as an antidepressant on 30 December 1985, and marketed under the name Wellbutrin. It is moreover considered as an atypical antidepressant, since it doesn't influence the serotonin levels. The Bupropion has been seen as more compelling than the SSRI's and is likewise used to expand the performance of SSRI's. The different side-effects of SSRI's have been abrogated by the utilization of Bupropion. The common side-effects as shown by the SSRI like weight gain & sexual dysfunction have not been shown by the use of Bupropion, rather it shows only isolated side-effects ^[19].

Bupropion is an antidepressant, which belongs to aminoketone class and is chemically related to tricyclic, tetracyclic, selective serotonin-reuptake inhibitors, or other known antidepressants ^[20].

Bupropion is an atypical antidepressant which acts as a nor epinephrine- dopamine reuptake inhibitor (NDRI) ^[21]. The various experimental researches related to the amendatory action and pharmacology of Bupropion Hydrochloride have been done till date, are summarized in table 1.

Table 1: Various studies conducted on Bupropion for its remedial action.

S.No.	AUTHOR	REVIEW	REPORT
1.	Ascher JA., et al. (1995)	Presented a review on the mechanism of antidepressant activity of Bupropion.	Basically discussion was carried out related to biochemical, in-vivo brain microdialysis, electrophysiologic etc studies done to analyse the possible mode of action of Bupropion. It was found to have noradrenergic action. The hydroxybupropion (a metabolite of Bupropion) have vital role in the antidepressant activity of Bupropion ^[22]
2.	Weihls KL., et al. (2000)	Conducted study on Bupropion sustained release versus Paroxetine for the treatment of depression in the elderly.	Elderly (>or=60years) outpatients with major depressive disorder were evaluated for 6 weeks by randomized, doubleblind study method, comparing Bupropion SR, 100- 300mg/day, & paroxetine, 10-40 mg/day. No, statistically significant differences were observed between the study groups. Because of the favourable side-effect profile of the Bupropion, it might provide a safe and effective nonserotonergic treatment alternative that is well suited as an antidepressant for the elderly ^[23]
3.	Slemmer J.E., et al., (2000)	Studied about the Bupropion as the nicotinic antagonist.	The study explained the interaction of Bupropion with nicotine and nicotine receptors. It was found that Bupropion blocks nicotine's antinociception, motor effects, hypothermia and convulsive effects with different potencies ^[24]
4.	Gadde KM., et al, (2001)	Conducted investigational study on the Bupropion for the weight loss to assess its efficacy and tolerability in overweight and obese women.	The randomized, double-blind, placebo-controlled comparison for 8 weeks was conducted on the selected subjects. They were administered with the Bupropion and placebo. It was observed that the Bupropion was more effective than placebo in achieving the weight loss in overweight and obese elder women ^[25]
5.	Gijsman H.J., et al, (2004)	Presented a systematic review on the evidence obtained from the randomized, controlled trials on the efficacy and safety of antidepressants used in short-term treatment of bipolar depression.	They included randomised, controlled double-blind trials for their study that compared antidepressant with placebo or alternative drug treatments. They conducted the trials to advocate the use of Bupropion as a first antidepressant choice for the bipolar depression ^[26]
6.	Stahl S.M., et al, (2004)	Reviewed the neuropharmacology of Bupropion as a dual norepinephrine and dopamine	They concluded that Bupropion acts via dual inhibition of norepinephrine and dopamine reuptake. The animal model

		reuptake inhibitor.	for depression showed that the administration of dopamine or norepinephrine-blocking drugs reduced the antidepressant effect of Bupropion [27]
7.	Dwoskin L.P., et al, (2006)	Reviewed the pharmacology and clinical profile of an antidepressant and tobacco use cessation agent i.e. Bupropion.	It was proved by the study that Bupropion attenuate the nicotine-induced unconditioned behaviours. The extensive metabolism of Bupropion produces three pharmacologically active metabolites, which showed the clinical profile. Being nAChR antagonist, Bupropion acted as antidepressant & tobacco use cessation agent [28]
8.	Wilkes S., et al, (2008)	Reviewed the use of Bupropion SR in cigarette smoking cessation.	It was found that the Bupropion acts by inhibiting the reuptake of Dopamine which is released due to the absorption of nicotine in the blood stream during cigarette smoking, which provides feeling of pleasure. Thus concluded the Bupropion as a first line agent alone or in combination with Nicotine Replacement Therapy for smoking cessation [29]
9.	Grunebaum M.F., et al.(2011)	Conducted study on the pilot randomized clinical trial of an SSRI vs Bupropion.	The study was carried out to understand the effect of drug on suicidal behaviour, ideation and mood in major depression. A double-blind, randomized, clinical pilot trial was conducted by taking Paroxetine or Bupropion for the patients suffering from DCM IV with suicide attempt history. It was finally concluded that suicidal behaviour and ideation would improve more with the Paroxetine [30]
10.	Calandra C., et al. (2012)	Conducted a retrospective cohort study on Bupropion vs Sertraline in treatment of depressive patients with binge eating disorder (BED).	The medical records of the outpatients diagnosed with depression and BED were selected for the study. Half of the patients were treated with the Bupropion 150mg/day and rest half of the patients were treated with Sertraline 200mg/day. Both drugs reduced the depressive symptoms and binge frequency but Bupropion showed a better effectiveness in reducing weight and improving sexual performances [31].
11.	Ravindran P.P., et al. (2015)	Studied the effect of bupropion and other antidepressants on body mass index (BMI).	The effect of co-medication i.e. Bupropion along with the six individual antidepressants on BMI using EMR based data analysis was studied. It was observed that Bupropion along with the SSRI acted as an augmentation therapy that targeted at an efficient therapeutic effect with minimal SSRI induced side-effects like weight gain, sexual dysfunction and emotional detachment

			[32]
12.	Bhatia M.S. (2015)	Conducted the study on Bupropion-induced stuttering.	The various neurotransmitters like Y-aminobutyric acid, serotonin and dopamine have been proposed in the pathogenesis of stuttering. It was observed that Bupropion was able to increase dopamine in the frontal cortex in the stuttering patient [33]
13.	Patel K., et al. (2016)	Reviewed and analysed the effectiveness of Bupropion as an antidepressant.	The meta-analysis of the drug was carried, by dividing in four categories: the sole use of Bupropion; Bupropion coprescribing; „other“ populations; and side-effects. The study revealed the superiority of Bupropion over placebo. Comparator trials showed the equivalence of effectiveness of Bupropion over other antidepressant [34]
14.	Elyasi F., et al. (2016)	Presented a case report on the acute dystonia after single dose of Bupropion.	The case showed the occurrence of dystonia due to Bupropion even with low doses and after a single dose. Concurrent use of Bupropion with a drug that affects serotonin reuptake or SSRI is likely to cause acute dystonia [35]
15.	Wasif N., et al. (2017)	Presented a case report on Bupropion-induced acute dystonia with dose escalation and use of Naranjo Nomogram.	This case reported that acute dystonia due to Bupropion occurred when an escalated dose of 150-300mg was daily administered. The concurrent use of Bupropion with SSRI might also cause the acute dystonia. The Naranjo Nomogram was a questionnaire which was designed to understand the likelihood of whether an adverse drug reaction is actually due to the drug rather than result of other factors [36]

ADVANTAGES OF BUPROPION:

BUPROPION has a unique pharmacology, inhibiting the reuptake of noradrenaline and dopamine, potentially providing pharmacological augmentation to more common antidepressants such as selective serotonergic reuptake inhibitors (SSRIs).

Unlike other antidepressants, Bupropion doesn't affect the user's libido, and it doesn't cause any weight gain as compared to other antidepressants. In fact, it is sometimes often prescribed along with other antidepressants to help counteract the sexual side effects of other medications.

It can be used as an adjunctive treatment to reverse the antidepressant induced sexual dysfunction and to elevate the efficacy of other antidepressant [37]. Bupropion is the first-line treatment for the tobacco cessation, which was approved by FDA in 1997 for its therapeutic use [38].

GENERIC BRANDS OF BUPROPION HYDROCHLORIDE:

The various brands of Bupropion are introduced by different companies of different strength and in varying dosage form^{[39], [40], [41]}. The generics of Bupropion which are equivalent to marketed brand of Bupropion i.e. Wellbutrin XL are being also introduced in the market^{[42], [43]}.

Table 2: List of 13 brands of generics of Bupropion Hydrochloride, manufactured by 9 companies.

S.No.	Brand name	Manufacturer	Dosage form	Strength
1.	Bupdep	Mediez Pharma Pvt. Ltd.	Tablet	150 mg
2.	Bupez SR	Aronex Life Science Pvt Ltd.	Sustained Release Tablet	100 mg
3.	Bupez SR 150	Cipla Limited	Sustained Release Tablet	150 mg
4.	Bupraset- XR (150 mg)	La Pharma	Extended Release Tablet	150 mg
5.	Bupron SR	Sun Pharmaceutical Industries Ltd.	Sustained Release Tablet	150 mg
6.	Ession ER	Psyco Remedies	Extended Release Tablet	150 mg
7.	Nicotex	Cipla Limited	Tablet	150 mg
8.	Nicotex SR	Cipla Limited	Sustained Release Tablet	150 mg
9.	Nicotex SR FC	Aronex Life Science Pvt. Ltd.	Modified Release Tablet	150 mg
10.	Smoquit-SR	Sun Pharmaceutical Industries Ltd.	Sustained Release Tablet	150 mg
11.	Unidep-SR 150	Consern Pharma Pvt. Ltd.	Sustained Release Tablet	150 mg
12.	Zyban	Glaxo Smithkline Pahraceuticals Ltd.	Tablet	150 mg
13.	Zyban 150	GSK	Prolonged Release Tablet	150 mg
14.	Forfivo XL	IntelGenxCorp	Extended Release Tablet	450 mg
15.	Aplenzin	Biovail Laboratories International	Extended Release Tablet	522 mg

Table 3: Other drugs that can be typically used in the treatment of depression in adolescence

DRUG NAME	STARTING DOSE (mg)	THERAPEUTIC DOSE RANGE (mg)
Fluoxetine	10	10–40
Escitalopram	10	10
Sertraline	25	25–200
Citalopram	10	10–40

ADVERSE EFFECTS OF BUPROPION:

Due to the high number of patients treated with BUP worldwide (more than 15 million have been estimated in the USA alone), a profile of adverse reactions associated to BUP has been established^[44]. In a review of three placebo controlled studies on BUP SR, Settle et al. identified that the most frequent adverse reactions (occurring in $\geq 5\%$ of the patients and more frequently than with the placebo) were headache, mouth dryness, nausea, constipation, insomnia and dizziness^[45]. From the clinical point of view, it is possible to observe exanthema-type allergic reactions, pruritus and rash and rarely anaphylactic/anaphylactoid reactions associated to the use of BUP^[46]. Lineberry et al., in 224 outpatients treated with BUP IR at fixed doses of 300 mg, only found four adverse events that occurred in more than 5% of the individuals of the group: headache (38% BUP vs 26% placebo); insomnia (23% BUP vs 7% placebo); dizziness (15% BUP vs 6% placebo) and nausea (13% BUP vs 10% placebo). None of these differences was statistically significant^[47].

CONCLUSION:

Depression is such mental issue that influences the complete way of life of an individual. It is found that it occur more often in ladies than in men. One out of each five ladies, and twelve men used to experience the ill effects of depression. It influences the psychological and passionate prosperity and at last influences the in general personal satisfaction. As indicated by the examination done for mental horribleness among the school youths, it was seen that as 29% of young ladies and 23% of young men languishing from depression were having this normal problem. The few types of burdensome issues are found, among which the most widely recognized are MDD and dysthymic disorder. Bupropion is one such key medication to this decimating mental issue.

It is the fourth most endorsed stimulant in the United States. It is moreover considered as an atypical antidepressant, since it doesn't influence the serotonin levels. Bupropion is the much requested medication among the young. In general, youth going through the period of depression might notice an improvement in different indications like improved mood, further developed focus, more energy and better sleep subsequent to taking this drug.

A once-daily dosing of Bupropion XL was created with the objective to further develop decency and consistence. Due to its interesting profile, bupropion has played and will keep on playing a significant job in the treatment of depression.

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