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DEVASTATING DEPRESSION OF YOUTH AND ITS REMEDIAL DRUG: A REVIEW

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ABSTRACT

Depression is the most common psychiatric disorder reported in every next person in today's lifestyle. Depression has become the third leading cause of global disease burden, and is accounting for 4.3% of total disability-adjusted life years. If this continues for long it will become the leading cause of disease burden by the year 2030. According to a community survey the prevalence rate of depression amongst the adolescents is between 1.8%-7.8%. The several forms of depressive disorders are found amongst, which the most common are major depressive disorder and dysthymic disorder. Amitryptyline along with a Selective Serrotonin Reuptake Inhibitor (SSRI), i.e. fluoxetine is the treatment option for depression, as per the list of essential medicines issued by the WHO. But because of the certain side-effects of SSRI's, it became necessary to switch on the bupropion to treat the condition of major depression. Bupropion was discovered in 1985 & is the fourth most prescribed antidepressant in the United States. The Bupropion was firstly discovered to treat the Major Depressive Disorder (MDD) and is frequently used for smoking- cessation. Bupropion is the much demanded drug among the youth. In general, youth undergoing through the phase of depression may notice an improvement in various symptoms like improved mood, improved concentration, more energy and better sleep after taking this medication.

KEYWORDS: Depression, Depressive Disorders, Bupropion, youth depression, smoking -cessation.

INTRODUCTION

Depression is the most common psychiatric disorder reported in every next person in today's lifestyle. According to an estimation by WHO, depression shall become the second largest illness by another decade in the world. It is found that the, depression more frequently occur in women than in men. One out of every five women and twelve men used to suffer from depression. This not only happens to adults but is also frequent in adolescents. Almost two percent of school children and five percent of teenagers suffers from depression, which usually goes unidentified. Mostly the people have wrong perception that all psychological disorders are related to depression. 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.[1]

Usually the patients of depression present themselves to psychiatrist with the complaints of medically unexplained somatic symptoms, or masked depression. Depression has become the third leading cause of global disease burden, and is accounting for 4.3% of total disability-adjusted life years. If this continues for long it will become the leading cause of disease burden by the year 2030. Depression is the common, treatable disorder which can continue for lifelong if not treated on time. It affects the mental and emotional wellbeing and ultimately affects the overall quality of life.[2]

Depression, a devastating condition for youth

Studies in the elderly suggest that, especially death in the family and financial problems are the most devastating events for depression and the same happens in the case of adolescents. Especially elderly females are in the capture of this dreadful psychic disorder.[3] The casual attribution of an individual is responsible for the nature of depression which is followed by the uncontrollable events.[4] According to a community survey the prevalence rate of depression amongst the adolescents is between 1.8%-7.8%.[5] From the past last two decades, depression has been encountered as a major mental health problem. 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.[6] The fig. 1 given below, explains the percentage of suicidal case amongst school going adolescents.[7]

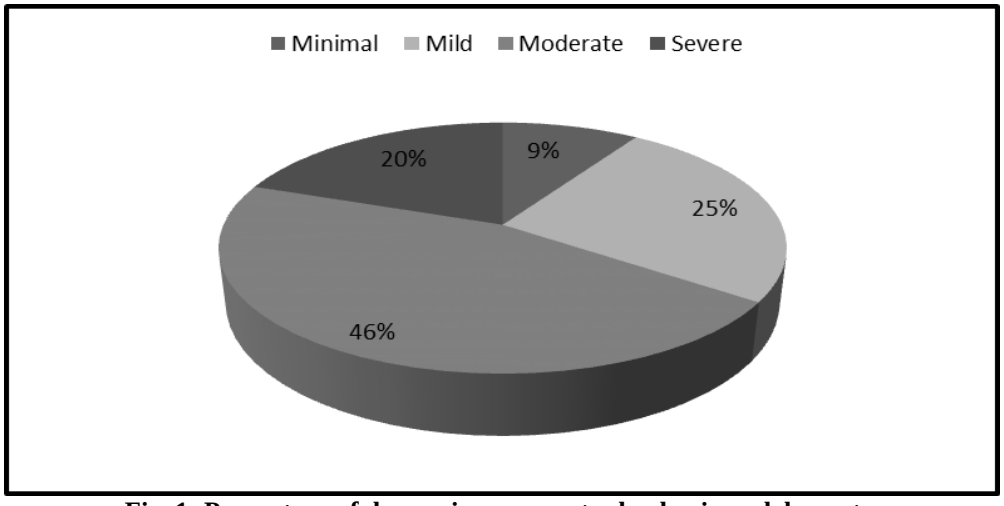

Fig. 1: Percentage of depression amongst school going adolescents.

An older adolescent (15-17yrs.) have 1.5-fold greater risk of depression as compared to younger adolescent (12-14yrs.). Parental mental health is also an important concern regarding the chances of occurrence of depression.[8] Another version of BDI which is used for measuring the depression in younger age group is known as Children's Depression Inventory (CDI).[9] Suicide has become the third leading cause of death amongst adolescents and young adults. Below figure is the representation of suicidal rates amongst male and female of different ages, (Fig. 2).[10]

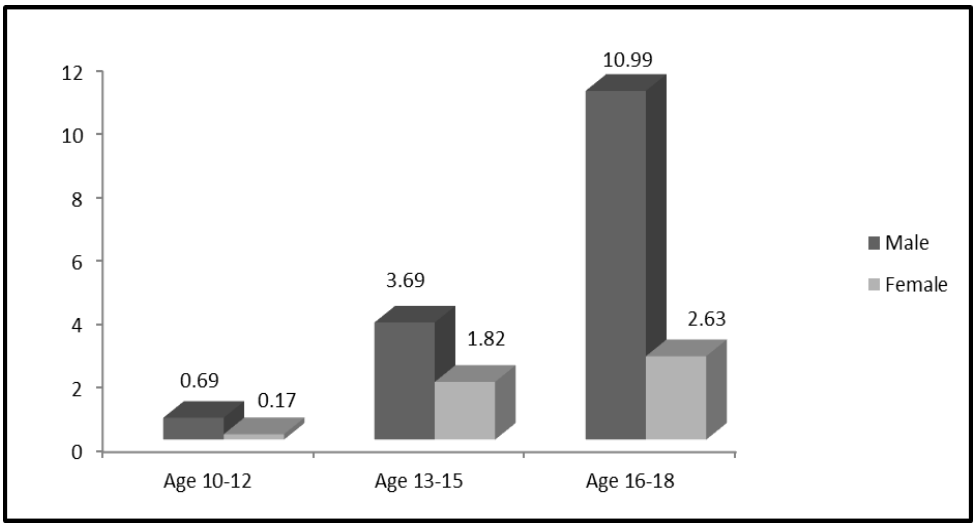

Fig. 2: Representation of suicidal rates in India by age ranging (10-18) & gender.

`Contributing factors for Depression

Beyond all other psychological factors, the major contributing factor that makes an individual vulnerable to depression is attribution style. It is responsible for maintaining the depressive symptoms once they develop.[11]

Although depression is agreed as a brain disorder by the scientists, but the debate continues on the appropriate factors responsible for this disorder.

The various factors that contribute to depression include:[12]

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

Types of Depression

Depression is observed as a heterogeneous disorder which is sometimes mistaken as single clinical mental disorder. The severity of depression may vary from individual to individual, i.e. from mild to extremely severe condition which includes psychotic depression having symptoms like hallucination and delusions.[13] The several forms of depressive disorders are found, amongst which the most common are major depressive disorder (MDD) and dysthymic disorder.

Major Depressive Disorder

This is commonly called as the **Major Depression** which is usually characterized by a combination of

symptoms which interferes with the person's ability to work, sleep, study or even enjoying pleasurable activity. Major Depressive Disorder has become global issue.[14] It is one of the complex disorders. The diagnostic criteria involves: depressed mood or apathy, loss of interest etc. For the proper treatment of major Depressive Disorder, it is necessary to provide the antidepressant medication for sufficient duration with sufficient dose and the patient must be monitored for the response and adverse drug reaction.[15]

➢ **Dysthymia**

This is a chronic disorder which has chances of occurrence in the substantial portion of population and it may also lead to the increased risk of Major Depressive Disorder. Dysthymia and Major Depressive Disorder shares several characteristics and also the response to pharmacotherapy but can be distinguished from one another on the basis of Hypothalamic-pituitary-adrenal (HPA) functioning. Dysthymia literally means to be in bad mood or ill- humour which is characterized by number of affective, neurovegetative and cognitive symptoms. This depressive disorder is more common in women than in men.[16]

➢ **Post-Partum Depression**

In many cases PPD remains undiagnosed and about 10-15% of new mothers are affected by it. The Post Partum Depression is basically the mixture of several "mood disorders", these mood disorders have several differentiating features, which are as follow:

- Baby Blues
- Postpartum Panic Disorder
- Postpartum Obsessive Compulsive Disorder
- Postpartum Post Traumatic Stress Disorder
- Postpartum psychosis.[17]

Types of Antidepressants

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.[18] Given below figure is the representation of the various types of antidepressants according to their generation, (Figure 3).[19],[20]

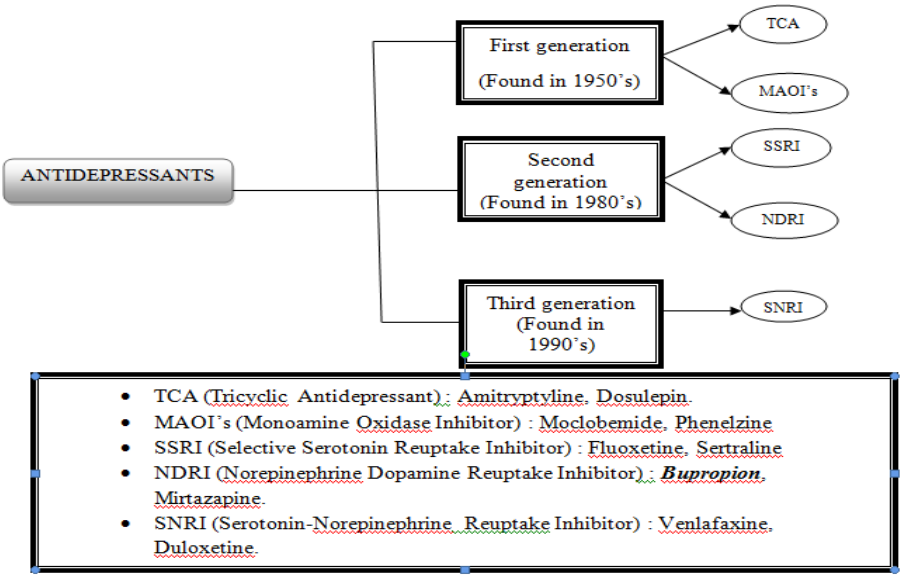

Figure 3: Flow chart with examples for various types of antidepressant.

Before the late 1980's, the treatment for depression was limited to TCA's & MAOI's. These categories are referred as traditional or first- generation antidepressants. But these drugs were found to be accompanied by multiple side-effects which were intolerable for the patient. TCA's tend to cause dry mouth & eyes & sometimes constipation, whereas, MAOI's shows hypertensive crises if taken along with some food or dietary supplement containing tyramine. So, to avoid these side-effects caused by the TCA's & MAOI's, amitryptyline along with an SSRI, i.e. fluoxetine is the treatment option for depression, as per the list of essential medicines issued by the WHO. But because of the certain side-effects of SSRI's, it became necessary to switch on the bupropion to treat the condition of major depression.[21]

Bupropion- A Key Drug to Depression

Bupropion was discovered in 1985 & is the fourth most prescribed antidepressant in the United States. It is also considered as an atypical antidepressant, since it does not affect the serotonin levels. The Bupropion has been found more effective than the SSRI's and is also used to augment the performance of SSRI's. The various associated side-effects of SSRI's have been abolished by the use 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.[20] The Bupropion was firstly

discovered to treat the MDD (Major Depressive Disorder) and is frequently used for smoking-cessation.[22]

Description & Pharmacological category

Bupropion is an antidepressant, which belongs to aminoketone class and is chemically nrelated to tricyclic, tetracyclic, selective serotonin-reuptake inhibitors, or other known antidepressants.[23] Bupropion is an atypical antidepressant which acts as a norepinephrine- dopamine reuptake inhibitor (NDRI).[24] The various researches related to pharmacology and the remedial action of Bupropion Hydrochloride have been done till now, which are summarised 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 microdylasis, 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.[25]
2.	Weihs 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, double-blind 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.[26]
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.[27]
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.[28]
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.[29]
6.	Stahl S.M., et al, (2004)	Reviewed the neuropharmacology of Bupropion as a dual norepinephrine and dopamine reuptake inhibitor.	They concluded that Bupropion acts via dual inhibition of norepinephrine and dopamine reuptake. The animal model for depression showed that the administration of dopamine or norepinephrine-blocking drugs reduced the antidepressant effect of Bupropion.[30]
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, Burpropion acted as antidepressant & tobacco use cessation agent.[31]
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 cigratte 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.[32]
9.	Grunebaum M.F., et al.	Conducted study on the pilot	The study was carried out to understand the effect of drug on

	(2011)	randomized clinical trial of an SSRI *vs* Bupropion	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.[33]
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 diagonosed 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.[34]
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.[35]
12.	Bhatia M.S. (2015)	Conducted the study on Bupropion-induced stuttering	The various neurotransmitters likeϒ-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.[36]
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: thesole 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.[37]
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.[38]
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 likelikhood of whether an adverse drug reaction is actually due to the drug rather than result of other factors.[39]

Benefits of Bupropion over other antidepressant

According to the Maurizio Fava et al., among all the newer antidepressants so far discovered, bupropion is having lower incidence of sexual dysfunstion, weight gain & somnolence. The efficacy comparison of Bupropion to the selective serotonin- reuptake inhibitors and other antidepressants, demonstrates it as an effective anti depressant. It can be used as an adjunctive treatment to reverse the antidepressant induced sexual dysfunction and to elevate the efficacy of other antidepressant.[40] Bupropion is the first-line treatment for the tobacco cessation, which was approved by FDA in 1997 for its therapeutic use.[41]

Journey of drug to sustained to extended release

Initially, the Bupropion was developed with the aim to improve on the safety & tolerability of previously developed antidepressants. This antidepressant is the only one among all antidepressants which is having dual action nor epinephrine (NE) & dopamine (DA) neurotransmitter system. After passing through several clinical trials for its safety and efficacy, the U.S. Food and Drug Administration (FDA) has approved Bupropion in 1989 and was introduced with the target to treat major depressive disorder. This was an immediate release (IR) medication. Based on the demonstration of the bioequivalence to the IR formulation, which required thrice-daily dosing, a sustained release (SR) formulation was developed and marketed in 1996. This formulation only required twice daily-dosing. But non-compliance was observed in the patients for this formulation compared to other SSRI (Selective Serotonnin Reuptake Inhibitors) because of their once daily dosing property; this propagated the development of extended release

formulation of Bupropion. This Bupropion XL formulation was approved in August 2003, which was having once- daily dosing and used for the treatment of major depressive disorder.[40]

Literature Survey for Bupropion Dosage Form

Boyong., et.al., (2003), developed the controlled release oral dosage form of Bupropion Hydrochloride by new pelletization process, typified by the application of a Bupropion/cellulose ether suspension to inert spheres and two unique formulations of sustained release coating which were applied to separate active drug pellets. The formulation acted as a membrane-controlled extended release in a pH- dependent manner. This improved the release rate of Bupropion.[42]

Chawla M., et al., (2005), investigated on extended release dosage form of bupropion hydrochloride and the process for its preparation. The dosage form included a core and a coating on core. The core part was having Bupropion Hydrochloride and optionally one or more pharmaceutically acceptable excepients and it was surrounded by the coating part which included water-insoluble film forming polymers, channelling agents, plasticizers etc. No osmotic enhancing agent was used in the core.[43]

Rampal A., et al., (2006), developed a solid dosage form that contains bupropion hydrochloride and glucono delta lactone or its corresponding open chain hydroxyl acid derivative. This solid dosage form could be in any of the form i.e. tablet, capsule or granulate with or without an immediate release profile, modified release profile or an extended release profile.[44]

Yang T., et al, (2006), worked on controlled release pharmaceutical oral dosage form and also embodied the invention to provide a method for preparing a controlled release dosage form comprising Bupropion or a pharmaceutically acceptable salt thereof. It consisted of the core and the enteric coating over the core, in which the core was comprised of controlled release matrix consisted of Bupropion, pharmaceutically acceptable salt or one or more pharmaceutically acceptable excepients, whereas the enteric coating was meant to provide the therapeutic effect for about 24 hrs after administration to a human patient.[45]

Wells L.M., et al, (2010), performed the investigation for dissolution rate increase on storage of Wellbutrin SR 100 mg tablets. The Wellbutrin SR 100 mg tablet was reformulated by using same ingredients and the same manufacturing unit process used for the original formulation. The reformulated tablet had a significantly slower initial dissolution rate and slower increase in dissolution rate on storage. By reformulating the product it was analysed that the hydrolysis of the release controlling polymer was occurring in the original formulation and that could be minimised by increasing the ratio of hypermellose to cysteine hydrochloride.[46]

Rasheed S.H., et al, (2010), performed their investigation on design and evaluation sustained release dosage form of Bupropion Hydrochloride and comparison with innovator product (Wellbutrin sustained release tablet). The wet granulation technique was used using HPMC and microcrystalline cellulose as a matrixing agent. The two different formulations (F-I & F-II) were prepared and the % cumulative drug release of the two formulations was compared with the marketed formulation. The % drug release of F-I & F-II were found to be 107.8% & 100.9% respectively whereas marketed formulation was having 103.0% cumulative drug release.[47]

Fouladi F., et al, (2012), developed a gastroretentive formulation of Bupropion Hydrochloride in the form of floating tablet. HPMC was used as a matrix material for designing tablet and appropriate blending was done with NaCMC to yield floating tablets with suitable drug release and swelling characterstics. Sodium bicarbonate was added as a gas-generating agent. Either of the two polymers (HPMCK4M & HPMCK15M) was used in different formulations together with either microcrystalline cellulose or lactose. Tablets prepared with MCC released ≥ 79% of the drug after 10 h, while those prepared with lactose released ≥ 85% of the drug within the same period.[48]

Tiwari S., et al, (2013), conducted their study on the effect of hydrophilic and hydrophobic polymer on sustained release matrix tablet of Bupropion Hydrochloride. The various polymers used for the study were HPMC K4M, HPMC K100M, Polyox WSR 303, Compritol 888 ATO, Precirol ATO 05 & Sterotex. The hydrophilic polymer tablets were prepared by direct compression method & hydrophobic polymer tablets were prepared by melt granulation technique. The *in vitro* dissolution study was carried in 900 mL Distilled water as dissolution media for 8h using USP dissolution apparatus II (paddle). Sterotex was found to be more release retardant among all hydrophobic polymer used. HPMC K100M acted as a good release retardant amongst all hydrophilic polymer used. The order of drug retard was HVO > Compritol > Precirol > HPMC K 100 M > HPMC K 15 > POLYOX 303.[49]

Deepika K., et al, (2014), formulated and evaluated Bupropion Hydrochloride sustained release tablets using combination of hydrophilic polymers. Optimization of the formulation was done by studying effect of drug to polymer ratio on drug release. The release of the drug was retarded by increase in the polymer concentration.[50]

Paudel A., et al, (2014), performed the study on formulation and *in vitro* evaluation of Bupropion Hydrochloride controlled release tablet. The tablets were prepared by using Guar gum, Eudragit RS 100, HPMC K15M, HPMC K100M at different concentration. HPMC K15M and HPMC K100M. The optimized formulations were compared with the marketed product for the

similarity and dissimilarity factor. The maximum drug release was shown by a formulation in which 25 mg of HPMC K15M was used i.e. 86.82% in 8hrs.[51]

Bupropion for youth

Bupropion is the much demanded drug among the youth. In general, youth undergoing through the phase of depression should notice an improvement in various symptoms like improved mood, improved concentration, more energy and better sleep.

The most potential benefit for taking Bupropion for youth is that, it does not cause addiction. It will not create "cravings" in the depressive patient like some people have for nicotine & other street drugs.[52]

Marketing Trends of Bupropion

Bupropion is a drug, which is used for the treatment of Major Depressive Disorder (MDD). For many years, Bupropion was marketed under the brand name "Wellbutrin". First immediate release was approved by FDA in 1985 as Wellbutrin-IR, which was followed by the sustained release formulation, approved in 1996 by FDA and marketed as Wellbutrin-SR. Later on, in 2003 FDA approved an extended release formulation which was marketed under the name of Wellbutrin-XL. The basis of approval of Wellbutrin SR & XL was the similarity of plasma level of Bupropion produced by these longer-acting drug products. In 2006, a XL generic version of Bupropion was marketed as Budeprion XL. This version was approved by FDA based on the evidence of bioequivalence study between brand and generic of bupropion.[53]

Bupropion is also marketed as Zyban, which was approved by FDA in 1997. The zyban is basically used for smoking cessation.[54]

Basically the name game for Bupropion was well-played by the GlaxoSmithKline (GSK). The company has given four different names to the same drug (Bupropion). Initially, it was marketed as Wellbutrin, an antidepressant and then relaunched as Zyban, a smoking-cessation aid. These two products shared an identical chemical structure but can be differentiated on the basis of marketing reasons. Now GSK has given a new name to the Wellbutrin, i.e. Prolev, and Zyban will be called as Quomem.[55]

List of Brands of Generics of Bupropion Hydrochloride

The various brands of Bupropion are introduced by different companies of different strength and in varying dosage form.[56],[57],[58]

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.	Bupep SR	Aronex Life Science Pvt Ltd.	Sustained Release Tablet	100 mg
3.	Bupep SR 150	Cipla Limited	Sustained Release Tablet	150 mg
4.	Bupraset-XR (150mg)	La Pharma	Extended Release Tablet	150 mg
4.	Bupron SR	Sun Pharmaceutical Industries Ltd.	Sustained Release Tablet	150 mg
5.	Ession ER	Psyco Remedies	Extended Release Tablet	150 mg
6.	Nicotex	Cipla Limited	Tablet	150 mg
7.	Nicotex SR	Cipla Limited	Sustained Release Tablet	150 mg
8.	Nicotex SR FC	Aronex Life Science Pvt. Ltd.	Modified Release Tablet	150 mg
9.	Smoquit-SR	Sun Pharmaceutical Industries Ltd.	Sustained Release Tablet	150 mg
10.	Unidep-SR 150	Consern Pharma Pvt. Ltd.	Sustained Release Tablet	150 mg
11.	Zyban	Glaxo Smithkline Pahrmaceuticals Ltd.	Tablet	150 mg
12.	Zyban 150	GSK	Prolonged Release Tablet	150 mg
13.	Forfivo XL	IntelGenxCorp	Extended Release Tablet	450 mg
14.	Aplenzin	Biovail Laboratories International	Extended Release Tablet	522 mg

List of Generic Version of Wellbutrin XL (Bupropion Hydrochloride- Tablet, Extended Release; Oral)

The generics of Bupropion which are equivalent to marketed brand of Bupropion i.e. Wellbutrin XL are being also introduced in the market.[59],[60]

Table 3: List of generics of bupropion which are equivalent to Wellbutrin XL and approved by the FDA.

Bupropion Hydrochloride- tablet, extended release ; oral			
S.No.	**Manufacturer**	**Approval Date**	**Strength(s)**
1.	TWI PHARMS INC	November 3, 2017	150mg, 300mg
2.	SINOTHERAPEUTICS INC	August 21, 2017	150mg, 300mg
3.	ANBISON LAB CO LTD	June 30, 2017	150mg, 300mg
4.	JUBILANT GENERICS	June 30, 2017	150mg, 300mg
5.	SCIEGEN PHARMS INC	April 12, 2017	150mg, 300mg
6.	LUPIN LTD	April 6, 2017	150mg, 300mg
7.	INVAGEN PHARMS	August 26, 2016	150mg, 300mg
8.	SUN PHARMA GLOBAL	December 18, 2014	150mg
9.	ZYDUS PHARMS USA INC	January 17, 2014	300mg
10.	WOCKHARDT LTD	November 21, 2012	150mg
11.	MYLAN	July 14, 2010	150mg, 300mg
12.	ACTAVIS LABS FL INC	November 26, 2008	150mg
13.	IMPAX LABS	November 26, 2008	150mg
14.	WATSON LABS INC	November 26, 2008	150mg
15.	ANCHEN PHARMS	December 14, 2006	150mg, 300mg
16.	VALEANT INTL	August 28, 2003	150mg, 300mg
17.	WELLBUTRIN (SR) of GSK	October 4, 1996	300-400 mg/d
18.	WELLBUTRIN (IR) of GSK	December 30, 1985	400-600mg

Table 3: List of generics of bupropion which are equivalent to Wellbutrin XL and approved by the FDA.

One of the patents was issued on August 1, 2000 for the delayed release tablet of Bupropion Hydrochloride.

CONCLUSION

Depression is such psychiatric disorder that affects the complete lifestyle of a person. It is found that the, depression more frequently occur in women than in men. One out of every five women, and twelve men used to suffer from depression. It affects the mental and emotional wellbeing and ultimately affects the overall quality of life. 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. The several forms of depressive disorders are found, amongst which the most common are MDD and dysthymic disorder. Bupropion is one such key drug to this devastating mental problem. It is the fourth most prescribed antidepressant in the United States. It is also considered as an atypical antidepressant, since it does not affect the serotonin levels. Bupropion is the much demanded drug among the youth. In general, youth undergoing through the phase of depression may notice an improvement in various symptoms like improved mood, improved concentration, more energy and better sleep after taking this medication. A once- daily dosing of Bupropion XL was developed with the goal to further improve tolerability and compliance. Due to its unique profile, bupropion has played and will continue to play an important role in the treatment of depression.

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