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A REVIEW ON ESTIMATION OF LORCASERIN HYDROCHLORIDE IN BULK AND TABLET DOSAGE FORM

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ABSTRACT

Obesity is a metabolic dysfunction associated with a wide range of chronic illnesses that cause significant increases in comorbidity and premature mortality, impaired quality of life and large healthcare costs. According to the World Health Organization, Obesity is a leading preventable cause of death worldwide, with increasing rates in adults and children. In 2015, 600 million adults (12%) and 100 million children were obese in 195 countries. Obesity is more common in women than men. These numbers are likely to increase exponentially in the future. Due to this scenario, it is important to highlight the available treatments for obesity and to assess their effectiveness. Although obesity is an ancient disease, studies are constantly being conducted to improve treatment effectiveness, reduce side effects of any current medications, and identify new therapeutics targets. Because the treatment of obesity is constantly evolving, treatment can be quite a challenge. Lorcaserin hydrochloride is use as antiobesity drug. Lorcaserin hydrochloride is available in tablet dosage form it is important to estimate this drug from dosage form. This review is focus on estimate of Lorcaserin hydrochloride in bulk and tablet dosage form by using RP-HPLC and UV Spectrophotometric method.

KEYWORDS: Lorcaserin Hydrochloride, RP-HPLC, UV-Spectroscopy.

1. INTRODUCTION:- Lorcaserin Hydrochloride

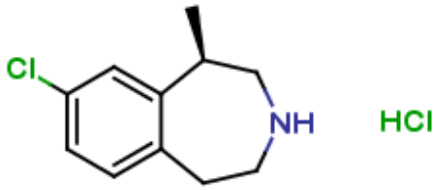

Figure 1. Chemical structure of Lorcaserin HCL.

Lorcaserin is chemically [1R]-8-chloro-2, 3, 4, 5-tetrahydro-1-methyl-1H-3-benzapine [12-13] and acts as a selective 5-hydroxy tryptamine (5-HT, serotonin) 2c receptor agonist which is developed particularly to aim human appetite expression.[5] Lorcaserin, a selective serotonin (5HT2c) receptor agonist is capable of suppressing appetite and food intake.[9] Induction of this receptor gives rise to a number of reactions that finally stimulates the release of 2-melanocortin stimulating hormone, which acts on melanocortin-4-receptors to control appetite.

Mechanism of action	Lorcaserin is pro-opiomelanocortin neurons stimulator present in the nucleus of hypothalamus resulting in a peak melacortin-4 receptor activity. This leads to satiety and decreased food intake.[14] Comparatively, Lorcaserin has a greater affinity towards 5-HT2C receptor than other 5-HT subtypes under recommended doses.[6]
Absorption	For oral administration, Lorcaserin has a better absorption from gastro-intestinal tract and its peak plasma concentration (Tmax) after a dose was found within 1.5 to 2 hours. Lorcaserin is highly soluble and highly permeable, meeting the criteria for Biopharmaceutics Classification System Class1. Lorcaserin is rapidly absorbed after oral dosing (Tmax, 1.5–2 hours) and has a plasma t½ of approximately 11 hours.[10] The availability of the drug in systemic circulation has not been determined exactly and no significance effect was found on peak concentration (Cmax). A study was conducted to describe the impact of food on absorption of Lorcaserin which was performed on 12 adult volunteers(6 men and 6 women) administered by single 10mg dose after eating high fat meal and during fasting. Results show an increase by 9% and 5% for Cmax area under the curve (AUC). This explains that there is no significant difference was found inpatient's drug administration after food intake.[10]
Distribution	The drug bounds of about 70% to plasma proteins and has good distribution in human central nervous system and cerebrospinal fluid.[6]
Metabolism	Lorcaserin is metabolized in the liver by multiple human cytochrome P450 enzymes and flavin-containing monooxygenase1.[10] Lorcaserin sulfamate (M1), N-carbamoyl glucuronide Lorcaserin (M5) and sulfate and glucuronide conjugates of oxidative metabolites was achieved by multiple enzymes pathway since it is independent to single enzymatic cycle.[6] The major circulating metabolite is M1 (inactive) but it accounts only for about minimum of 3% administered dose in urine and another inactive form of metabolite M5 was found to be have maximum metabolism in urine.[6]
Excretion	About 92 % was eliminated primarily in urine and rarely through feces (2.2%).
Dose	An oral dose of 10 mg is recommended to give twice a day with or without food. In

	patients with renal failure, dose adjustment is not necessary. And use of Lorcaserin is not recommended in patients with severe renal failure. Discontinue if 5 % weight loss is not achieved by week 12.[14]
Dosage form	BELVIQ – Each tablet contain 10mg of Lorcaserin Hydrochloride Hemihydrates.[11] BELVIQ XR – Each tablet contain 20mg of Lorcaserin Hydrochloride anhydrous extended release.[11]
Adverse effects	The most common effects include vasodilator effects such as hypertension, headache, and dizziness.[8] Various adverse effects listed alphabetically by body system and by decreasing frequency within body system are; Body as a whole: pain Gastro-intestinal system: Nausea, Vomiting, Diarrhea, and Constipation. Respiratory system: Cough, sinus congestion.[6] Reproductive system: Urinary tract infection. Post marketing adverse effects such as rashes and back pain are also reported.[6]
Contraindications	Contraindication can be seen with concomitant of potent CYP3A4 inhibitor (e.g. Ketoconazole) and CYP2D6 inhibitor (e.g. Quinidine).[6]
Warnings and Precautions	Valvular heart disease: If sign or symptoms develop consider to discontinue Belviq and evaluate the patient for possible valvulopathy.
Use in specific populations	Nursing Mothers: Discontinue drug Pediatric Use: Safety and effectiveness not established and use not recommended

1.1 Drug profile of Lorcaserin Hydrochloride (Table 1)

Lorcaserin Hydrochloride	
Category	Anti-Obesity
Synonym	(1R)-8-chloro-1-methyl-2,3,4,5-tetrahydro-1H-3-benzazepine 8-chloro-2,3,4,5-tetrahydro-1-methyl-1H-3-benzazepine APD 356, AR-10A, Belviq, Lorcaserin
Chemical formula	C11H15CL2N
IUPAC Name	(5R)-7-chloro-5-methyl-2,3,4,5-tetrahydro-1H-3-benzazepine;hydrochloride
Molecular weight	232.148 g/mol
Characteristic	Off-White to Pale Yellow Solid
Solubility	Chloroform, Ethyl acetate, Methanol, H2O, Acetonitrile, DMSO
Log P and pKa	2.56 and 9.53
Melting point	99°C, >212
Storage	Hygroscopic, -20°C Freezer, Under inert atmosphere
CAS No.	846589-98-8
Indication	For the treatment of obesity, as an adjunct to a reduced-calorie diet and increased physical activity.

2. Reported Method is categorized depending on the following considerations

Sr. No.	Drug	Method	Description	Ref.No.
01	Lorcaserin HCL , Metoprolol	HPLC based Bio analytical method	**Column:** Phenomenex Luna C18 column (250×4.6 mm i.d, 5 µ particle size) **Mobile Phase:** phosphate buffer (pH3):acetonitrile: methanol (65:20:15) **Flow rate:** 1.0 ml/min. **Wavelength:** 222 nm **Retention Time:** 5.15 and 7.19 min **Linearity range:** 500 to 3000 ng/ml	01
02	Lorcaserin HCL	HPLC based content determination	**Column:** Waters XBridge C18(3.5 µm, 4.6×150mm) **Mobile Phase:** 0.1 % trifluroacetic acid aqueous solution and 0.1 % trifluroacetic acid acetonitrile solution (80:20) **Flow rate:** 1.0 mL/min. **Wavelength:** 220 nm **Content of Lorcaserin HCL:** 99.57%, 99.24%,99.61% **Temperature:** 40 ^{0}C **Linear range:** 40~ 100 µg/mL	02
03	Lorcaserin HCL	HPLC and Thermodynamic investigation	**Column:** Chiralpak IA Column **Chiral Stationary phase:** Immobilized with amylose tris (3.5-dimethylphenylcarbamate) chiral sector Mobile Phase: n hexane/ethanol/ methanol/diethylamine (95:2.5:2.5:0.1,v/v/v/v) **Flow rate:**1.2 mL/min **LOD:**0.45 **LOQ:**1.5 µg/mL **Temperature:** 20 ^{0}C to 50 ^{0}C	03
04	Lorcaserin and Carbamazepine	UPLC-MS-MS based on plasma and brain tissue sample	**Column:** Acquity BEH^{TM}C$_{18}$ (50×2.1 mm,1.7 µm) **Mobile phase:** acetonitrile-10 mM ammonium acetate-formic acid (85:15:0.1,v/v/v) **Flow rate**: 0.25mL/min **MS-MS-** ion transitions: m/z 195.99>143.91 for Lorcaserin and m/z 237.00>178.97 for IS **Linear range:** 1.08-500 ng/mL in plasma and 3.07-500ng/ml in brain tissue.	04

3. CONCLUSION

- There is least number of RP-HPLC, UV and Stability indicating methods are reported on Lorcaserin hydrochloride.
- The RP-HPLC method consists of different mobile phase and column.
- Through the study of this article selection of wavelength can be easy and accurate.
- Not only wavelength can also give brief idea of mobile phase.

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