"Formulation, Development And Evaluation Of Immediate Release Tablet Of Eletriptan Hydrobromide An Antimigraine Drug"

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Abstract

This research aims to develop and assess an immediate release tablet of the antimigraine drug, a potent medication for migraine relief. Various formulation strategies were explored to achieve a rapid start of action and improved compliance from the patient. Several criteria were assessed for the prepared tablets, including drug content, disintegration time, dissolution profile, and stability. The optimized formulation exhibited promising characteristics, suggesting its potential as an effective treatment option for migraine patients. Migraine immediate-release tablets are designed to provide immediate relief from migraine symptoms. Most of these include drugs such as sumatriptan, zolmitriptan or rizatriptan, and Eletriptan, which acts as a vasoconstrictor constrict blood vessels in the brain and block pain pathways. These tablets are designed to be taken at the start of a migraine attack for quick relief. The immediate-release tablets were made with Eletriptan hydrobromide as the active pharmaceutical component. The direct compression method was used together with the proper excipients to create the tablets. Several formulation parameters were adjusted to achieve the desired drug release kinetics, disintegration time, and mechanical strength. Among other things, the tablets' thickness, hardness, friability, disintegration time, and in vitro drug release were evaluated. All things considered, the recently developed Eletriptan hydrobromide immediate-release tablets serve as an effective treatment choice for the acute management of migraine, improving patient compliance and providing prompt relief from migraine symptoms.

Keywords: *Potent, Sumatriptan, Zolmitriptan, rizatriptan, Eletriptan, Vasoconstrictor*

1. INTRODUCTION

A pulsating sensation in one area of the head is a common way that migraine headache pain manifests itself. But there's more to it than that; the IHS categories migraines according to their intensity and frequency of episodes, in addition to additional symptoms

including light and sound sensitivity and vomiting. Women have migraine three times as frequently than men do, and it impacts more than 10% of the global populace. A number of factors, such as stress, anxiety, hormone fluctuations, bright or flashing lights, deprivation of food or sleep, and food ingredients, can cause recurrent episodes in migraine sufferers. Certain women may experience migraines as a result of changes in hormone levels during their menstrual cycle[1].

Migraine is a disease that is not recognized by the headache, usually attached to one side, the attacks for 4 to 48 hours with frequent nausea, vomiting, weakness to lights and sounds, flashes of light, laziness, movements and other signs. The two main types.

1. Migraine with aura
2. Migraine without aura

1. Migraine with aura: headache occurs before vision or other neurological symptoms.
2.Migraine without aura- In which pulsatile dilation of certain large cranial vessel is the immediate causes of pain[2].

Classification of antimigraine drugs

Antimigraine medications to prevent Various medications are used for migraines, including triptans, beta-blockers and ant convulses, methysergides, calcium channel blockers, antidepressants, clonidine (-blowers), pizotifen and their analogues; these drugs are also known as anti-inflammatory[3].

Drug therapy of migraine

The choice of migraine medication should depend on the individual's strength and frequency of anticonvulsant attacks and the patient's response to previously used medications.

Mild migraine

If you experience headaches less than once a month but can concentrate on a headache that lasts up to 8 hours. drug therapy of mild migraine simple analgesics / NSID S or their combinations

Moderate migraine

A moderate migraine can be classified as mild and the chest pain is more severe and lasts from 6 to 24 hours, nausea/vomiting and other symptoms are more pronounced and debilitating the role of the patient. More than one attack per month. drug used in the moderate migraine is NSIDs combinations / a Triptans / ergot alkaloids

Severe headaches

These patients experience severe headaches two to three times a month that last 12 to 48 hours, often accompanied by dizziness, vomiting, and other symptoms. The subject is very weak during the attack. Medications used to treat acute pancreatitis include triptans/ergot alkaloids + prophylaxis, propranolol/other inhibitors, amitriptyline/other tricyclic antidepressants, flunaizine/other Ca channel blockers, and valproate/topiramate. Some migraine medications.

Ergotamine

This is the most effective type of ergot given at the start of a migraine attack, so rescue doses are needed. It can be administered after a few hours.

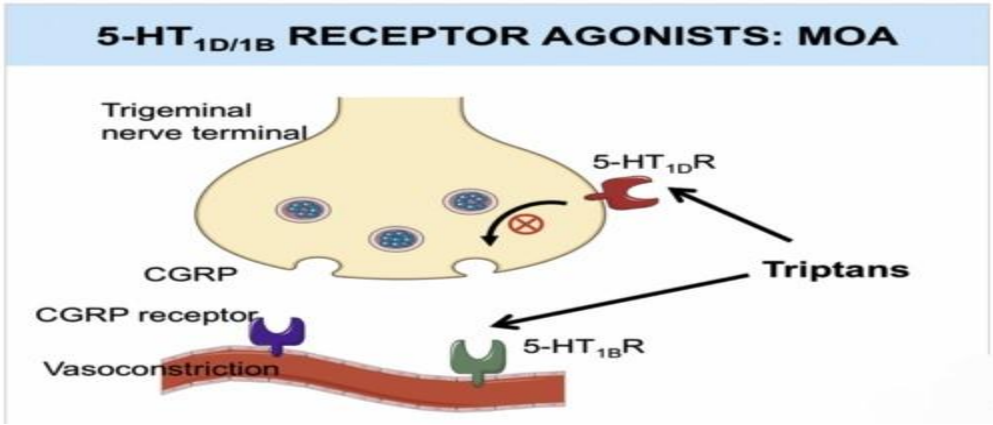
Dihydroergotamine

Injected DHE is almost as effective as parenteral administration because it is less risky**.**

Figure no 1 Drugs used in treatment of migraine

Mechanism of triptans

Due to their Affinity to the 5-HT1B- and 5-HT1D-Serotonin-Receptors, triptans have the ability to prevent Migraines. When triptans connect to vascular 5-HT1B-receptors, the cranial arteries compress and cause pain, which is the reason for migraine-attacks.04



Mechanism of triptans fig no 2

HT1D/1B agonists (triptans)

Triptans are mediated by 5HT (1B/1D) receptors, which causes the constriction of damaged cerebral vessels and the inhibition of release of vasoactive neuropeptides by the Cranial nerve

and forbid neurotransmission. There are many types of triptans on the market, such as sumatriptan, almotriptan, Eletriptan, frovatriptan, naratriptan, rizatriptan and zolmitriptan.

Eletriptan
5HTA, 5-HTE, 5-HT2B, and 5-HT7 receptors are mildly affinized for Eletriptan; 5-HT2A, 5-HT2C, 5-HT3, 5-HT4, 5-HT 5A, and 5-HT6 receptors are little to non-affinities for etriptan; and 5-HT1B, 5-HT1D, and 5-HT1F receptors are highly affinized for etriptan. The pharmacological activity or affinity of etriptan at opioid, muscarinic, dopaminergic D1 or D2, adrenergic alpha1, alpha2, or beta, and adrenergic receptors is minimal.

To explain why 5-HT1 receptor agonists are so successful in treating migraines, two theories have been proposed. One idea proposes that vasoconstriction, which is associated with the alleviation of migraine headaches, is caused by the activation of 5-HT1 receptors found on intracranial blood vessels, particularly those on the arteriovenous anastomoses. According to the alternative theory, inhibition of sensory nerve terminals in the trigeminal system occurs when 5-HT receptors are activated.

A class of tryptamine medications known as triptans is used as an anticonvulsant to treat cluster headaches and migraines. In the 1990s, this medication gained popularity. While it works well for treating certain headaches, it is not regarded as a cure and does not offer prophylactic care. It's Not useful for relieving other kinds of pain, such as headaches. The following symptoms can be alleviated with triptans:

- Light and Sound Sensitivity
- Headache;
- Nausea and vomiting[4]

2. MATERIALS AND METHODS

Table no 1. Material used in Manufacturing

Sr. No	Ingredient	Functions	Grade	Source
1	Eletriptan Hydrobromide	Active Ingredient	-	Nuland Lab
2	Lactose Monohydrate	Binder	Super tab 11 D	DEF Pharma
3	Microcrystalline Cellulose	Diluent	Avicel 101	FMC Biopharma
4	Crosscarmellose Cellulose	Super Disintegrant	Ac-di-sol	Hyqual
5	Sodium Starch Glycolate	Super Disintegrant	Primogel	Hyqual
6	Magnesium Sterate	Lubricant	-	Avantor
7	HydroxyPropylmethyl Cellulose	Film Former	Hypromelose E5	Hyqual
8	Titanium Dioxide	Opacifier	-	Hyqual
9	Triacetin Dioxide	Plassticizer	-	Sensient
10	FD&C Yellow no 6/sunset Yellow FCF	Colourant	-	Sensient

	aluminium black			

Manufacturing Method

An approach known as direct compression was used to create the 40 mg Eletriptan hydrobromide immediate-release tablet. A development lab-scale trial was carried out to determine the parameters of the manufacturing process, including blending, compression, and coating, based on the target product profile, an assessment of the physiochemical properties of the drug substances and other ingredients, a review of the literature, and the scientific procedure carried out prior to the manufacturing process. Producing a product with an appropriate in vitro dissolving profile was the ultimate goal of the study[5].

Selecting the Excipients:

Selection of excipients for a formulation is based on the basic process used to create the tablets. The selected process, which involved direct compression and a literature study, was taken into account when selecting the excipients. According to their grade, physical characteristics, and qualities, the inactive excipients were selected. All excipients employed in the development trials are suitable for use in direct compression. The stability research results for the API and its suitability for the recommended inactive excipients bolstered the choice of formulation composition.

Steps in Manufacturing:

Manufacturing Process is As Follows:

Step.1. Dispensing[6]

The following materials were dispensed: polyvinyl pyrrolidone, magnesium stearate (Hyqual), lactose monohydrate (SuperTab SD11), microcrystalline cellulose (Avicel PH105), croscarmellose sodium (Ac-Di-Sol SD 711), and API.

Step.2. Sifting[7]

API Polyvinyl pyrrolidone, lactose monohydrate (SuperTab SD11), microcrystalline cellulose (Avicel PH105), and croscarmellose sodium (Ac-Di-Sol SD711) were separated and sieved through sieve #50 before being packed in individual polybags.

Separate magnesium stearate (Hyqual) particles were sorted through a #50 screen and then placed in a polybag.

Step.3. Blending and Lubrication[8]

The material that had been sifted from step 2 above was mixed for 15 minutes at 10 rpm in an octagonal blender. We lubricated step no. 3 for five minutes at 15 rpm in an octagonal blender using Hyqual, the sifted magnesium stearate from step 2.

Step.4 Direct Compression[9]

Compression was performed on the lubricated mix from the previous phase using a compression machine and the proper punch tooling to create the tablet.

Step.5. Coating[10]

After adding Opadry white to the purified water and agitating the mixture for 35 minutes. The mixture was filtered through #100 mesh. The coating solution of the coating machine was applied to the core tablets from step 5.0 until a weight gain of 3.00% by wt was attained.

Table no 2. Formulation Chart

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
	Quantity of mg per Tablet								
Eletriptan Hydrobromide	20	20	20	20	20	20	20	20	20
MCC PH105				25	40	40	40	43	43
Hydroxypropyl methyl cellulose		20	30						
Lactose monohydrate	80	60	50	55	40	40	40	35	45
Cross carmelose sodium					4		4	5	5
Polyvinyl pyrrolidone	4	4	4	4			1	2	2
Sodium starch Glycolate						4			
Magnesium stearate	3	3	3	3	3	3	2	2	2
Total wt.	107	107	107	107	107	107	107	107	107
Opadry white	3	3	3	3	3	3	3	3	3

3. RESULT AND DISCUSSION

1.Organoleptic properties:

Table no 3. Organoleptic Properties

Properties	Observation
Colour	White to light brown
Taste	Bitter
Odour	Odourless
Appearance	Crystaline Powder

3.Solubility:
Several solvents (both aqueous and organic) were used to test the API sample's solubility. It's only a qualitative analysis. Thus, the following outcomes were attained:

Table no 4. Solubility Study

Sr.No.	Solvent	Solubility
1	Alcohol and Water	Completely soluble
2	Methylene chloride	Very little soluble

4. Particle size determination: -

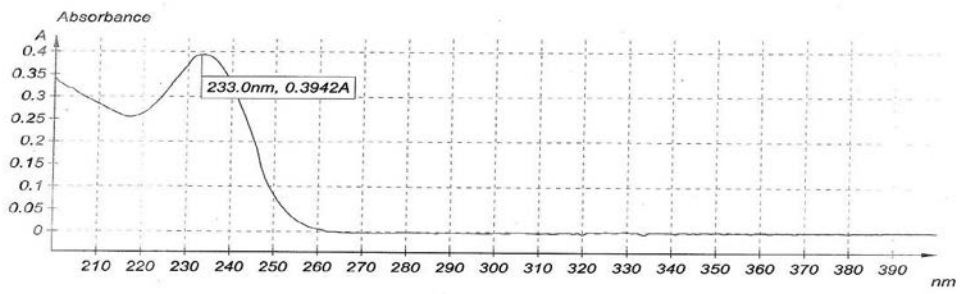
The Malvern particle size analyzer was used to evaluate an API sample, and the following size ranges of particles were discovered:

Table no.5.Particle size data

Sr. No.	Diameter	Particle size(µm)
1	D10	11.6
2	D50	55.8
3	D90	172.3

Ultraviolet absorption spectroscopy:

Wavelength Selection:



Calibration curve:

Using a UV spectrophotometer, a solution with varying concentrations of Eletriptan hydrobromide was produced and scanned at 233 nm. Plotting the graph of absorbance vs concentration, it was discovered to be linear between 2 and 10 µg/ml, showing that it complied with Lambert and Beer's law.

Table no 6 . wavelength Selection

Sr.No.	Concentration (µg/ml)	Absorbance
1	0	0
2	2	0.190
3	4	0.281
4	6	0.400
5	8	0.564
6	10	0.724

Table no.7.Selected wavelength

Sr.No.	Parameter	Finding
1	Wavelength Identification	233 nm
2	Regression equation	y = 0.0699x-0.0119
3	Correlation coefficient	R^2 = 0.9996

BCS Solubility Analysis:

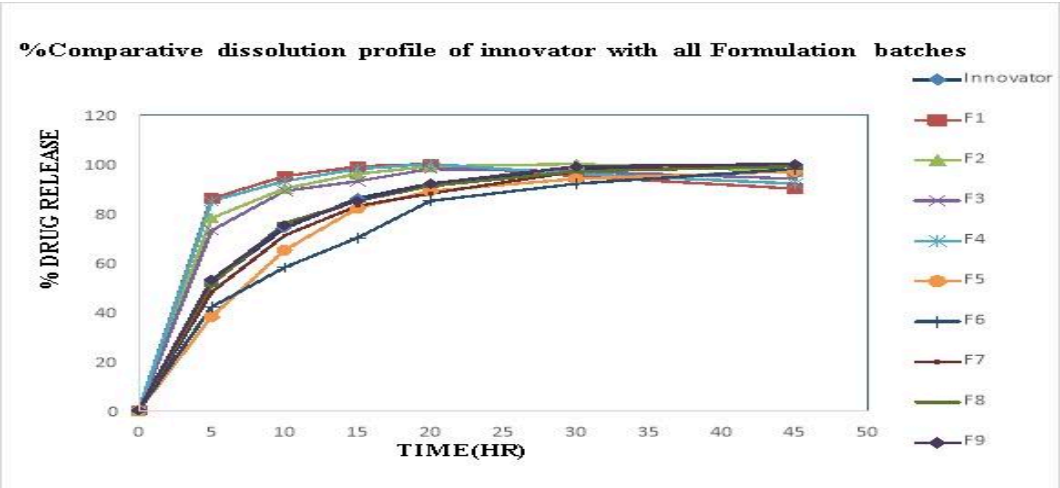
Table no 8: Solubility study Data

Sr. No	Media	mg/250ml
1	Purified Water	853.0
2	0.01N HCl	1905.0
3	0.001N HCl	2114.5
4	0.1N HCl	731.0
5	pH 6.8 phosphate buffer	979.2
6	pH 4.5 Acetate buffer	1148.1
7	pH 7.5 phosphate buffer	578.6

In vitro Dissolution Study:

Table.9: % Comparative dissolution profile of the innovator with all formulation batches in 0.1N HCl

Media	900 ml of 0.1 N HCl in a USP Type I apparatus spinning at 100 rpm (Basket)									
Time	% Drug Release HCl									
	innovator	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0	0
5	52	86	78	73	85	38	42	48	51	53
10	74	95	90	89	93	65	58	71	76	75
15	86	99	96	93	98	82	70	83	85	85
20	92	100	99	98	100	89	85	88	91	92
30	98	95	100	97	96	94	92	97	97	99
45	100	90	97	94	92	97	98	100	99	100



From the above result it was observed that the innovator can meet the Q point i.e. 85% drug release within the 15 min.

4. CONCLUSION

Eletriptan hydrobromide was used to create a stable and reliable dosage form, and the creation, development, and assessment of an immediate-release tablet of the "anti-migraine drug" was the goal of the investigations. Hydrobromide Eletriptan Comparable dissolving results were observed in the instant-release tablet made by direct compression compared to the reference product. A USP Type I (basket) solvent was used for the evaluation of all eight formulations for in vitro drug release, with each formulation being tested for 30 minutes at 100 rpm. The novel product's dissolving profile was compared to the batches' dissolution profiles. The novel product's in vitro dissolving profile was similar to lot F8, out of the five lots. Phosphate buffers with pH values of 6.8, 7.5, and 4.5 were used for multimedia leaching. The improvement in dissolving rate over that of the reference product was noted and found to be a satisfactory outcome. The fact that the superdisintegrant had an impact on the tablet's release rate was discovered. According to the results above, batch F8 demonstrated a result that was equivalent to the innovator's while also demonstrating an improvement in the dissolving rate when the superdisintegrant was used. This suggests that the increase in solubility eventually leads to an increase in bioavailability. Thus, it is possible to produce immediate-release pills of the anti-migraine medication Eletriptan hydrobromide with proper results.

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