2. Need of Work

U.S. Patent No. 5,466,699 mentioned a class of chemical compounds, indolyl compounds for the treatment and prophylaxis of migraine, known as triptans. All the triptans are selective 5HT1-receptor agonists employed for the treatment of migraine headache. Today there are seven triptans namely Eletriptan, Frovatriptan, Sumatriptan, Zolmitriptan, Naratriptan, Rizatriptan and Almotriptan have been marketed.

Triptans are specific and selective agonists for the 5-HT 1 receptors. Sumatriptan binds to 5-HT 1D receptors, Zolmitriptan, Rizatriptan, Naratriptan, Almotriptan and Frovatriptan bind to 5-HT1B/1D and Eletriptan binds to 5-HT 1B/1D/1F receptors.

Mechanism of action for triptans is supposed to vasoconstriction effect on carotid arterial circulation without affecting cerebral blood flow, peripheral neuronal inhibition and inhibition of transmission through second order neurons of the trigeminocervical complex.

The 5HT1-receptor mediates vasoconstriction and thus modifies blood flow to the carotid vascular bed. 5HT1-receptor agonists are beneficial in the prophylaxis and treatment of disease conditions wherein vasoconstriction in the carotid vascular bed is indicated, for example migraine, cluster headache and headache associated with vascular disorders, collectively termed as "migraine".

All the triptans have been formulated for the treatment of acute migraine. Out of different triptans the Almotriptan malate possesses the highest oral bio-availability with least side effect and fast onset of action followed by Eletriptan and Sumatriptan, accordingly.

Study of migraine treatment proves that conventional tablet of Almotriptan malate relieved the pain or headache in the patient but after 2 hrs the recurrence of headache may occur in many patients. Many patients have a recurrent migraine in the day, and only one such recurrence in a day can be treated with a second dose of triptan.

Sustained release tablet formulation over an extended period of 24 hrs would greatly relieve recurrent migraine. Sustained release formulation also reduced the frequency and severity of migraine associated nausea and/ or phonophobia at baseline along with, somnolence, paresthesia, and dry mouth which will not offered with the conventional
drug delivery. Oral administration Almotriptan results into fast onset of action and rapidly relieve the pain or headache.

The adverse drug reaction incidence associated with G. I. disturbances and nervous system likes dizziness and somnolence are enhanced with the single large dose of Almotriptan malate as compared to lower dose. Hence, the Almotriptan malate sustained release formulation help to reduce the same.

The present investigation pertains to formulation of sustained release tablet of Almotriptan malate. The present research work deals with the oral administration of triptans that can deliver a therapeutically effective dose of a triptan for an extended period of time for at least 24 hrs.

Almotriptan malate marketed under the brand name Axert with strength of 12.5 mg. The literature review revealed that Almotriptan malate were formulated for oral, sublingual, buccal, parenteral (e. g. subcutaneous, intramuscular or intravenous), rectal, topical and intranasal administration.

Oral administration is most commonly employed and acceptable route of drug delivery for and by the patient. Single preparation of sustained release drug delivery system may achieve the desired medicinal effect with more efficiency and longer duration than multiple dosages of the same drug and dose. The goal of these systems is to supply optimal concentration of a drug for a longer time than conventional system.

The therapeutic efficacy of orally administered Almotriptan malate had shown rapid onset of action, with significant headache relief in moderate to severe attacks of migraine with or without aura.

Trigeminal sensation during the migraine leads to the development of highly painful condition like cutaneous allodynia. Allodynia refers to a condition in which pain produced by usually non painful stimulus. Allodynia is established in 90% patients suffer from the migraine attacks. Allodynia is only prevented by treating the patient with triptan like Almotriptan malate at early phase or when migraine occurs.

The proposed work involves designing & optimization of Almotriptan malate sustained release tablets will overcome the drawback of conventional drug delivery system and confer the following advantage-

- Improved patient convenience and compliance
Need of Work

- Reduced recurrence of migraine
- Relieve headache associated with migraine with or without aura
- Decreased tempo of migraine associated nausea and phonophobia
- Improved efficiency in treatment
- Reduced frequency of drug administration
- Maintained constant drug blood levels

For sustained release systems, the oral route of drug administration has, by far, received the most attention as it is natural, uncomplicated, convenient and safer route. Oral sustained release drug delivery systems formulated using direct compression method is proved to be useful in the pharmaceuticals for its ease of formulation, enhanced stability, faster production, avoid degradation by moisture and/or thermal treatment and hydrolytic or oxidative reactions occurred during processing of dosage forms. Sustained or controlled release drug delivery system prepared by entrenched drug within a polymer matrix that may be natural, semi-synthetic or synthetic in nature. The sustained release polymer is combined with the drug or other active ingredients in such a way that the active ingredient is released from the material in a predetermined and at constant rate for desired time.

Hence present research work focused on the preparation of sustained release dosage form by using the matrix polymer alone and in combination and by using the different techniques employed for the preparation of same. In current work three different approaches are used to formulate the sustained release tablet.

**Matrix tablet by direct compression**

The matrix tablet prepared by direct compression requires fewer unit operation processes, less machinery, reduced number of personnel, less processing time, improved product stability and increased production rate. Matrix tablets containing drug and release retarding material i.e. polymer offered the straightforward approach in designing a sustained release system.

**Hot melt granulation**

Waxes have been extensively investigated for sustaining the release of drug. They provide several advantages include good stability at varying pH ranges and effectively retard the water soluble drug. Hence the aim of the present study is to develop a
controlled release solid oral dosage form using hydrophobic waxes for sustained release of drug\(^6\).  

**Liquisolid technique**  
It is suggested that liquisolid technique has the potential for reduce drug dissolution rate and thereby formulation of sustained release system of highly water soluble drug. If hydrophobic carriers used instead of hydrophilic carries in liquisolid systems, sustained release systems can be obtained with constant dissolution rates (zero order release) irrespective to the solubility of the drug candidate. It is also economical for both patient and industry perspective as production of liquisolid system is analogous to that of conventional tablets formulation.