Abstract

Title of thesis: Formulation Development of Solid Oral Dosage Form

The aim of present research work is to prepare the novel sustained release formulation of drug used in the treatment of migraine. Triptans are selective 5-HT/1D receptor agonist which mediates vasoconstriction and thus modifies blood flow to the carotid vascular bed and relieve the migraine. 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 and such recurrence in a day can be treated with a second dose of triptan. Hence sustained release tablet formulation over an extended period of 24 hrs shall 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 of Almotriptan has shown results into fast onset of action and has rapidly relieved the pain or headache. The adverse effect associated with G. I. disturbances and nervous system like dizziness and somnolence which are prominent with the single large dose of Almotriptan malate as compared to lower dose.

Hence, the Almotriptan malate sustained release formulation helps to overcome the same. Therefore, in the present research work it is assumes to reduce the problem associated with the conventional therapy. The literature review revealed that Almotriptan malate were formulated for oral, sublingual, buccal, parenteral, rectal, topical and intranasal administration but oral sustained release formulation of Almotriptan malate is not reported. Hence in present research work an attempt is made to formulate the Almotriptan malate sustained release formulation by using the different approaches viz. matrix tablet, liquisolid compact and melt granulation technique.

UV and HPLC analytical method development and validation is carried out for the Almiotriptan malate as per the ICH guidelines by using QbD approach. The analytical
performance parameters such as linearity, range, precision, and accuracy, limit of detection and limit of quantification, sandell’s sensitivity and molar absorptivity were analyzed.

The method was developed successfully and study showed that the developed HPLC method is simple, rapid, accurate, and precise. The HPLC analytical method with UV detection has been successfully developed for the determination of Almotriptan malate in active pharmaceutical ingredient.

Selection and procurement of drug and excipients was followed by the preformulation study to describe the suitability of drug and excipients in formulation development. Characterization study concludes that the procured sample of drug and excipients were pure in nature. The drug excipient compatibility depict that no physical or chemical interaction between the drug & polymers were seen and having compatibility with each other.

The preformulation study followed by selection of excipients for the sustained release formulation carried out by sustained release formulation by using Plackett Burman design. The matrix tablet formulation was developed by using central composite design. The HPMC and Carbopol shows the prominent result in sustaining the drug release. The QbD principle helps in more robust formulation development for matrix formulation with predefined quality.

The liquisolid technique was successfully employed for the formulation of sustained release compacts of Almotriptan malate. It is concluded that liquisolid technique has the potential to retard drug dissolution rate of highly water soluble drug by employing hydrophobic carriers with constant dissolution rates of highly soluble drug. The hot melt granulation technique used for the sustained release formulation development shows pH independent solubility and effectively retards the release of water soluble drug. The $3^2$ full factorial design was successfully employed for the development and optimization of sustained release hot melt tablets. The used hydrophobic waxes in combination with sustained release polymer effectively sustained the drug release.
It is concluded that the ANOVA and experimental design can be successfully employed for the formulation development and optimization as well as for excipient selection. QbD approach is productively used for the formulation development. The target selection by QTPP, identifying the CQA of sensitive TPP, risk assessment of CQA, production of design space for high risk factor and define the control strategy results into development of more robust formulation with predefined target. Stability data shows that the morphological, physical and chemical properties of prepared formulations were remain unchanged indicating that the developed formulations were stable for the entire period of stability study and having good shelf life.

Finally, it is concluded that the sustained release tablet of Almotriptan malate prepared by using liquisolid technique is the excellent formulation among all the formulation as it follows zero order release i.e. the drug dissolution is independent on the concentration of drug. The SR tablet is formulated efficiently with the aid of QbD approach and design of experiment. The drug release is sustained effectively for 24 hrs with predefined targeted product profile by successfully employing different approaches of formulation development.