ABSTRACT

The pellets are dosage forms which deliver the drugs safely to the body and in pelletization technique materials are changed to spherical shape which can flow easily. Pelletization is famous well defined previous technique. Different pelletization techniques now used in pharmaceutical industries are conventional pan coating, fluid bed technology, centrifugation and extrusion-spheronization. Methods mentioned above have some drawbacks such as pan coating technique which is mostly applied because of its low charge of installation but it required trained personnel and it consume time with less product yield. Pellets give excellent therapeutic benefit on single unit formulation when given in capsule, disintegrating tablet or suspension forms. Pellets can be used in the supply of drugs by controlled released technique. Pellets are flexible to design and formulate in dosage form with enhanced safety and efficiency of biological preparations. Pellets prevent the higher localized concentration of the medicament.

The actual intention behind the work was to sustain the drug release profile by using different coating agents in various concentrations on non pariel seeds containing NSAID’s (celecoxib, etoricoxib, aceclofenac) for the treatment of arthritis.

At the beginning of the study thorough literature review was done. Drugs, non pariel seeds and polymers were procured from the different pharmaceutical manufacturers. Standard calibration curves for the drugs were plotted and preformulation studies were done comprising Hausner’s ratio, physical appearance, tapped density, solubility, bulk density, Carr’s index and melting point. Conventional coating pan was used for preparation of drug loaded pellets and for coating purpose. Formulated pellets were evaluated for angle of repose, % moisture content, bulk density and sieving. The in vitro medicament release, % drug loading and the friability detections were the further test in a line to be performed.

Scanning electron microscopy, FTIR, DSC and kinetic model fitting studies were performed on finalized and optimized batches. Lastly pellets were filled in capsules containing diluent MCC (Avicel PH101) and lubricant talc. The prepared batches of capsules were evaluated for general appearance, content of actives, weight variations, content uniformity and in vitro dissolution studies. Stability study was done at 40°C±2°C/75%RH ±5% RH and the samples were taken off and detected for the in vitro drug release characteristics, appearance and drug content at the end of first, second and third months.
The preformulation study was conducted on the non pariel seeds before going to actual formulation. It was found that all the non pariel beads were white colored and found to be odorless. The bulk density executed by the non pariel seeds was 0.78 gm/ml. It was viewed that the non pariel beads illustrated the tapped density of 0.84 gm/ml. The friability for the non pariel seeds was identified as 0.04%. The non pariel beads depicted Carr’s index as 13.10%. The drug was found to be odorless and off white powder having 0.65 gm/ml bulk density. The medicament showed 0.82 gm/ml of tapped density and 134–135°C melting point.

The etoricoxib pellets showed % moisture content in between 2.11% to 2.47%. The particle size analysis was performed by the sieving technique. The formulated pellets were found to be in range of 702-720 micron size. The angle of repose was detected in between 9.44-11.21°. Friability of all the batches was found to be less than 1%. No broken pieces or particles of pellets were seen after the completion of test and hence it was concluded that the pellets were bear the sufficient mechanical strength and absorbed the shocks occurred during handling and transportation.

Batch AF4 was illustrated 21.54% drug loading. As the pellets were spherical in shape the flow property was found to be excellent. Batch AF4 was optimized based on in vitro dissolution evaluations and showed 92.56% cumulative drug release. USP dissolution apparatus II was employed for the in vitro study. SEM study was revealed that coating was uniform and surface of pellet was smooth. The FTIR study was proved that no incompatibility in drug and polymers was existed and the composition was stable. DSC study revealed that etoricoxib medicament was not reacted with the added material of formulation. The optimized batch follows the first order release kinetic. The formulated pellets were filled in to the empty capsules of size 00 containing MCC and talc. The final weight of the capsules was kept at 520 mg. All the capsules were free from deformities and found to be smooth and fine with good appearance. The optimized batch of capsule showed the 98.24% active ingredient. The capsules were passes the tests for actives, weight variation and uniformity of content. The Batch AF4 released 92.15% cumulative drug in 12 hr of dissolution study. After three months of stability study it was found that the appearance and texture of all the capsules were satisfactory and fine. The batch AF4 of capsules illustrated drug content as 94.27% at the end of 3rd month. The obtained results proved that all the capsules were showed the adequate content of medicament at the end of 3rd month. The percent cumulative removal of medicament was found to be 87.34% in last month.
Second choice of drug in present study was celecoxib. Standard calibration curves for celecoxib were sketched out. The graph was found to be linear in between absorbance and concentration and obeyed Beer Lambert law. The celecoxib powder was found to be white off colored with free from odor. The drug showed solubility in organic solvents and solublized in ethanol and methanol. The medicament showed 0.55gm/ml bulk density, 0.42gm/ml of tapped density and 14.12% Carr’s index. The drug powder showed 1.19 Hausner’s ratio and 157- 158°C melting point.

The limit of 2.10 % - 2.90% moisture content was identified for the formulated batches. When observed by sieving method formulated pellets were detected in 694-716 microns size range. The reading of less than 0.5 % was obtained for the friability of pellets. The bulk density of the formulated pellets batches was present in the range of 0.71 gm/ml -0.81 gm/ml with 0.80 gm/ml to 0.86 gm/ml tapped density. In between 9.44 to 11.48 the repose angle was present. It was found that batch AF4 illustrated 20.98mg% of drug. The in vitro dissolution study was performed in triplicate and batch AF4 released 91.33 % of medicament in 12 hr of study. As the released pattern of batch AF4 was best suited to the present designed research work and hence was optimized. During SEM study it was seen that all the pellets have smooth surfaces with free from cavities and deformities. No roughness was seen on the surface of pellets. In IR findings no interactions of medicament and used polymer were detected. Hence it was proved that the composition was stable and suitable for administration through orally. It was detected in DSC work that the celecoxib medicament was not reacted with the added material of formulation. It was confirmed from model fitting study that batch AF4 follows first order release having highest 0.989 kinetic value as compared to other models.

The empty hard gelatin capsules were filled by mixing the measured quantity of medicament containing pellets with talc and Avicel PH101. The final weight of the capsule was kept at 540mg. It was found that all the capsules have good transparent appearance with smooth and fine texture. Neither deformity nor pinholes were found on the surfaces of capsules. The batch AF4 showed the 98.09% active ingredient. The batch of capsule passes the weight variation and content uniformity tests. It was seen that the optimized batch of pellets after filling in capsule released the 91.34 % of cumulative medicament in 12 hr of dissolution of work. The capsules were passes the stability test with 94.11% drug content and 87.37% drug release at the end of 3rd month.
The last drug of choice in present study was aceclofenac. Standard calibration curves for aceclofenac were prepared and follow Beer Lambert law. The preformulation studies on aceclofenac medicament were conducted.

The aceclofenac pellets demonstrated moisture content in level of 2.11 % - 2.43%. The formulated pellets were found to be in range of 708-725 micron size. In the limit of 0.71 gm/ml - 0.80 gm/ml the prepared pellets batches were illustrated bulk density. The tapped density was detected as 0.80 gm/ml to 0.86 gm/ml with 9.25°-11.58° angle of repose. The friability for all the batches of pellets was identified to be less than 1%. Batch AF5 showed the 21.22% drug loading. Batch AF5 released 92.34% of medicament in 12 hr of dissolution work. It was also observed that the released pattern of batch AF5 was best suited to the present designed research work and hence was optimized.

SEM study showed that all the pellets have smooth surfaces. It was also examined during the study that the pellets were free from deformities and cavities on their surfaces. No interaction among the employed polymers and medicament was seen in FTIR. Nil incompatibility was observed in between medicament and added materials in DSC work. It was confirmed from model fitting study that batch AF5 follows first order release having highest 0.978 kinetic value as compared to other models. It was identified that all the capsules were smooth and possessed fine texture with good transparent appearance. The content of drug in optimized batch of capsule was found to be 98.15%. The capsules were passes the weight variation and content uniformity tests. It was detected that the optimized batch of pellets after filling in capsule liberates the 93.39 % of cumulative medicament. Neither deformities nor pinholes were found on the surfaces of capsules after the stability study. The drug content and in vitro dissolution of capsules of AF5 batch were detected up to the 94.10% and 86.12 % respectively at the end of 3rd month.

It was concluded that OD dose of capsule containing sustained release pellets of medicament for the treatment of arthritis could be prepared by the method utilized in current work. The technique employed in the research work was economical and for the industrial purpose could be scale up.