SUMMARY AND CONCLUSION
Preparation of sustained release pellets was done in present piece of research containing NSAIDs for the treatment of arthritis. Over the traditional utilized single unit preparations i.e. capsules and tablets pellets were shown many inherent benefits. In experimental work the coating pan in which composition of medicament and Eudragit RS 100 in isopropyl alcohol was employed on the surfaces of non pariel seeds. For spraying the liquid the spray gun has to be utilized. The speed of rotation of pan was adjusted at thirty rotations in a minute. The gun should be moved properly so as to avoid localized over wetting of pellets surfaces. Three baffles were provided inside the revolving pan for easy moment of pellets. The pellets were then transferred to the hot air oven which was set at the temperature of $40^\circ$C. The pellets were kept inside an oven for three hours so that all moistures removed completely and another film of sustained release material applied easily on them. The drug loaded pellets were then added in to the conventional pan as used before. In the isopropyl alcohol the Eudragit RL 100 was dissolved to obtain the solvent of coating. Di butyl phthalate was incorporated in the formula of coating solution as a plasticizer. The coating solution was formulated in various concentrations. Manually the solution was sprayed on medicament containing pellets with the help of gun. At $40^\circ$C in hot air oven the drying was done for three hours.

The drugs of choice for study were etoricoxib, celecoxib and aceclofenac. Firstly, etoricoxib medicament was selected and standard calibration curves were prepared and graphs were plotted. The graphs found to obeyed Beer Lambert law. 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. When examined through compound microscope the non pariel beads were observed to be completely spherical in shapes. As the non pariel beads possessed macroscopic structure hence could be seen through open naked eyes and viewed as circular in shapes. 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 instrument Roche friabilator was employed for the examination of friability of non pariel seeds. The friability for the non pariel seeds was found to be 0.04%. As friability was found to be less than 1% and hence concluded that all pellets were bear the sufficient mechanical strength. No broken pieces or particles of non pariel seeds were seen after the completion of test. It was proved from the friability study that non pariel seeds were also easily bear the shocks occurred during the
coating procedure. The Carr’s index for the non pariel seeds was obtained as 13.10%. From the findings of Carr’s index it was proved that non pariel seeds possessed excellent flow characteristics. After the preformulation study on non pariel seeds the same study was done on etoricoxib drug. The drug was found to be odorless and off white powder having 0.65 gm/ml bulk density. For the measurement of bulk density by the cylinder it was essential to dry and calibrate it. While measuring bulk density it was also necessary that the cylinder must not be disturb or tap. It was observed that if tapping was given to the measuring cylinder then it would affect the quality of results. It was also essential during the study that pellets should not be compacted, if compacted then it altered the accuracy of results. In other words it could be said that bulk density was represented by the loose packing of poured sample within the cylinder and without the consolidation of sample. The medicament showed 0.82 gm/ml of tapped density. In tapped density the sample was tapped till its original volume was changed and it attained the constant volume. The sample was illustrated 134- 135°C melting point. It was observed from the melting point study that compound was exactly melted at the same stated temperature of 134-135°C and hence it could be declared that the medicament was pure. The reading of 15.19% was viewed by the medicament for the Carr’s index. To count the interaction within interparticle the Carr’s index has to be utilized. Carr’s index has wide application before formulation of dosage form and hence included in preformulation studies. It gives an idea about material’s flow ability. It was found that if sample was freely flowing then it’s tapped and bulk densities values were very near to each other and hence the reading of Carr’s index was also found to be less. Same way if the sample flow poorly then interaction within the interparticles was more and value of tapped and bulk densities was obtained more leading to higher Carr’s index. As the etoricoxib medicament showed 15.19% Carr’s index it could be said that the flow feature possessed by the powder was good. The reading of 1.20 was observed for the Hausner’s ratio and it could be said that pellets possessed the good flow quality. The Hausner’s ratio was utilized to count ability of flow of the powder in the preformulation study of dosage form. Same way the Carr’s index was also utilized to obtained the flow ability of powder.

The obtained results of % moisture content were present in between 2.11 % to 2.47%. Batch AF2 showed least amount of % moisture content i.e. 2.11% and batch AF8 showed highest amount of % moisture content i.e. 2.47%. All prepared batches were dried in an oven at the temperature of
110 ±5 °C till sample attained the constant weight. It was observed that all the batches of pellets has acceptable limit of moisture content.

The sieve technique was utilized for the particle size analysis. The sieving method was widely used technique in the preformulation study of tablets and capsules. It was necessary that no coating was done on the surfaces of sieves. All necessary steps were taken to keep the surfaces of sieves clean and dry so as to avoid the possibility of interaction among the sieve and material to be sieved. The important parameters which affected the results of sieving were period of shaking and weight of pellets. The formulated pellets were found to be in range of 702-720 micron size.

It was found that sieving was simple and economical method and performed at the laboratory level. In case of sieving method the results obtained were rapid and reproducible. It was also noted that those particles with particle size below 50 µm were not be analyzed by this method. The mechanical shaker holding the sieves must shake the pellets for 20 minutes. Decreased in timing of vibration less than 20 minutes was produced the inaccurate results. It was reported during sieving study that pellets were colloided with one another leading to attrition. The attrition phenomenon was resulted in breaking of pellets and affects the accuracy of results. As the pellets possessed the sufficient friability (less than 1%) and hence such kind of attrition phenomenon was not noted during sieving study.

It was identified that the bulk density was lies in the limit of 0.71 gm/ml -0.82 gm/ml for the manufactured batches of pellets. Batch AF2 showed the least bulk density among the prepared batches i.e. 0.71 gm/ml. Batch AF7 showed the highest bulk density among all formulated batches i.e. 0.82 gm/ml. It was concluded from the bulk density study that all pellets of prepared batches showed bulk density less than 1gm/ml. The experiment will not be conducted till the glass measuring cylinder get washed twice perfectly and dried to overcome any possible cross contamination with the material to be examined. If the cylinder was not clean then the adhered particles in the inside surface of cylinder may get mixed with the actual material.

It was clearly identified that the tapped density of all the formulated batches of pellets was present in the limits of 0.81 gm/ml to 0.86 gm/ml. The batches AF2, AF6 and AF15 depicted 0.81 gm/ml of tapped density and it was the least found density among all the batches. The batch AF4 and AF7 showed 0.86 gm/ml of tapped density and it was the highest tapped density among all the formulated batches.
The angle of repose was detected in limit of 9.44-11.21°. It was also found that the pellets were must dried properly in an oven at mentioned temperature and time (40°C for 3 Hr), because improper drying of coated pellets may leads to clogging of aperture of funnel. It was also marked during study that the pellets flow feature was detected to be excellent if repose angle value is lesser. As mentioned inside the literature that if sample possessed irregular and rough surfaces then the angle of repose was found to be more for that sample. Less reading of angle of repose was attained by the pellets due to their smooth and even shape surfaces. It was also marked during the experiment that if lubricant was added in less quantity then it affects the quality of results and decreased the repose angle of sample. Same way if the quantity of added lubricant was enhanced then it improved the value of repose angle for that sample.

The friability value for 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 pellets bear the sufficient mechanical strength and absorbed the shocks occurred during handling and transportation. The percent loading of medicament on the pellets surfaces was estimated by spectrophotometerically at 254nm. The drug loading for etoricoxib medicament was lies between 19.05% to 21.54%. Batch AF4 was illustrated 21.54% of drug loading where as batch AF1 showed 19.05% of drug loading. As the pellets were spherical in shapes the flow property was found to be excellent for them.

On the basis of dissolution study parameters batch AF4 was optimized which showed 92.56% cumulative release of medicament. USP dissolution apparatus II was employed for the in vitro study. For etoricoxib pellets, hydrochloric acid of 0.1N having pH1.2 was used where as for celecoxib and aceclofenac capsules, phosphate buffer (pH 7.4) was utilized. It was observed that paddle revolved smoothly and not produced any kind of wobble. The sample was kept at the bottom of dissolution container before the start of experiment. The necessary gap of 25± 2mm was also kept among the base of vessel and blade bottom. The shaft was inserted inside the vessel in such a fashion that its axis was at the distance of 2mm from the vertical axis of container. It was also found that paddle and shaft possessed inert properties because prior coating was present on their surfaces. SEM study was performed on batch AF4 pellets and it was revealed that coating was uniform and surface was smooth. After the FTIR study it was proved that no incompatibility in drug and polymers was existed and composition was stable. From the Table of interpretation it was cleared that all the important and essential sharp peaks were
viewed in the sample pellets. Different types of liquids, solids and gases can be analyzed by the help of infrared absorption spectroscopy. The area used by the FTIR is from 4000 to 400 $^{-1}$. So many inorganic and organic materials showed absorption radiation in this limit of 4000 to 400 $^{-1}$. The FTIR instrument has very large accuracy in case of wave number. The chances of errors with the instrument was very rare and negligible i.e. $\pm 0.01 cm^{-1}$. The instrument has enormously higher resolution of $0.1 \sim 0.005 ^{-1}$.

The FTIR contains the interferometer and it was the big differentiating point from other spectrophotometer. The interferometer divides the single beam of light in twice and hence rout of both the beams became different. The interferometer then rejoined the both the beams of lights and conduction on them was carried out within detector. The detector counts the intensity difference of both the beam with respect path difference. The interferometer has one beam splitter and two mirrors. Among the two mirrors one was fixed while other was movable. Beam splitter passed only half light and reaming half light was reflected by it. Reflected and transmitted lights were hits by the movable and fixed mirrors. The mirrors reflected back both the light beams and they rejoined with one another at the point of beam splitter.

In DSC evaluations the eudragit RS 100 material gave peak at 217.98$^0C$. Same way eudragit RL 100 illustrated peak at 263.78$^0C$. It was clearly seen from the thermogram of pure etoricoxib medicament that it was melted at the 139.72 $^0C$. The standard melting point for etoricoxib mentioned inside the literature is 134$^0C$- 136$^0C$. The formulated pellets of etoricoxib depicted sharp endothermic peak at 133.16 $^0C$ which was equivalent to the pure drug melting point. After doing comparison it was seen that the etoricoxib medicament in pellets having coat of eudragit RS 100 and eudragit RL 100 was not diverged from standard melting point of medicament as mentioned in literature. Another very sharp peak which was observed in formulation thermogram at 219.16$^0C$ was of eudragit RS100. It was concluded that the etoricoxib medicament was not reacted with the added material of formulation. Hence the preparation of etoricoxib pellets was said to be stable.

Materials like Graphite, alumina, copper and platinum was used for the construction of pans. The pans were selected accordingly to stay away from cross reaction among sample and pan. Depending up on different DSC models the size of sample was chosen from 0.5 mg-10mg. The operation of DSC was taken place with constant pressure and hence flow of heat was equals to alteration in enthalpy. The nitrogen gas was blown on the sample to be examined to generate dry
and reproducible environment. Due to presence of nitrogen gas the chances of oxidation of material was reduced. The apparatus which was employed in doing the current DSC work was Mettler Toledo, Germany.

Depending up on the various functions and material to be examined the DSC are now available in various designs. The basic requirement which should be present in DSC apparatus is that it should be capable to assess the slight variation in temperature by maintaining stable rate of heating and cooling. The apparatus must performed perfect temperature examination. It was also essential that the machine should perfectly observe the variation in flow of heat among the reference and sample so as to obtain good base line with reduction in noise. Nowadays completely automatic machines are available in market equipped with devices which clean and load the material and wok in relation with the computer to load the sample. Cleaning and degassing of sample was also to be performed with the help of computer. These types of computer operated machines have capability to check the fifty samples per day with great precision and negligible error. The machine is competent enough to heat the material up to $600^\circ$ C and hence sample might be decomposed during heating process. Due to decomposition of material there might be release of harmful gases may takes place. Proper arrangement should be made for the emission of dangerous gases. It was advisable that material never be heated more than their temperature of decomposition. It was marked that at room temperature the liquid nitrogen starts to boil and hence wearing of gloves, shoes and goggle was highly advisable. Before doing actual DSC work material must be dried and clean perfectly to obtained accurate and sharp peaks. Forceps was used to add the material in pan and to put the pan lid on sample. Calibration should be conducted to get the best possible results. The pans must be clean and dry properly to avoid the cross contamination. If by default contamination was happened then it defiantly affects the accuracy of results. Preparation of sample a critical and most important step in DSC and hence material must be loaded very curiously inside the pan with the help of forceps only. Before going to actual experiment both the pan were checked for remained solvents and moisture of last reading. Heaters were observed to check whether they are providing heat to the reference and material equally. Speed of heating and cooling must be examined perfectly. The selection of quantity of material must be done properly and higher amount should not be added in to the pan. The whole operation must be examined keenly to avoid errors occurred during
processing. During addition of material in a pan it was good to keep it thinner and it should not be compressed. Cutting of sample was good practice to gain sample having thin size.

The optimized batch follows the first order release kinetic. The model of zero order kinetic depicted 0.962 reading and 0.973 for Higuchi model. The value of Hixon Crowel model was obtained to be 0.967. The value showed by the Korsmeyer Peppas model was 0.977. It was confirmed from model fitting study that batch AF4 follow first order release having highest 0.986 kinetic value as compared to other models. In first order kinetics the speed of process linearly enhanced with the enhancement in amount of medicament and the process was depend on amount of medicament. The formulated pellets were filled in empty capsules of size 00 containing lubricant talc and diluent MCC (Avicel PH101). After suitable calculation of required dose of medicament the necessary active excipients i.e. talc and MCC were added. The laboratory motor must be washed with water and cleaned properly before the start of experimental work. Care should be taken while filling the capsules so as to maintain uniformity of weight. Final evaluation tests were carried out on filled capsules. It was necessary that disposable hand gloves must be use during handling of capsules so as to avoid any possible interaction or contamination of product. The platform on which the filling and sealing operations was carried out must be kept clean and free from dust. The procedure carried out at room temperature. The filled capsules were immediately sealed and packed in aluminium pack. The concentration of talc must be kept below 5% because it was used in formula as a lubricant. It is found in literature that increased in the quantity of talc more than 5% will exchange its function from lubricant to filler. Hard gelatin capsules were easy to fill and dispense. As the pellets were spherical in shapes they were filled up easily in empty capsules. The final weight of capsules was kept at 520 mg. All the capsules were free from deformities, smooth and found with good appearance. The optimized batch of capsules showed the 98.24% active ingredient. The study was performed in triplicate manner for achieving the best possible results.

The weight variation test was performed on selected 20 capsules. It was found that from the average weight no capsule was deviated by higher than 7.5%. It was also seen that no single capsule was diverged by higher than two times from the same percentage limit. It was declared that capsules passed the test for weight variation. It was found that all the ten selected capsules meet the specification as given in Indian Pharmacopoeia and passed the content uniformity test.
for them. It was found that there was good drug uniformity in all the ten capsules and uniform drug content was detected in all of them and showed drug content in between 95%-100%. The Batch AF4 released 92.15% cumulative drug in 12 hr of dissolution study. The same apparatus was used for the in vitro dissolution work as used previously for the pellets.

The process of dissolution was carried out at temperature of 37°C ± 0.5°C. It was detected that enhancement in temperature beyond 37°C±0.5°C improved the process of dissolution of medicament inside the dissolution fluid. It was seen that the process of liberation of medicament through the system was also affected by the speed of paddle. Increased in the rate of rotation of paddle higher than 100 rpm was boost up the process of release of medicament from pellets.

The stability study on the formulated capsules was successfully conducted at 40°C±2°C/ 75% RH ±5% RH up to three months. The samples were evaluated for each month for appearance, drug release and content of drug. After three months of stability study it was detected that appearance and texture of all the capsules were fine. There were no deformities and pinholes on the surfaces of capsules. The drug content of capsules of batch AF4 which was 98.24% at the beginning of study came gradually up to 94.27% at the end of 3rd month in stability study at the condition of 40°C ±2°C / 75% RH ± 5% RH. The obtained results proved that all capsules showed the adequate content of medicament at the end of 3rd month. In each month the dissolution work was performed on the optimized batch of capsules up to the three months. The percent cumulative removal of medicament was found to be 90.10% at the end of first month. At the end of second month it was found to be 88.22% and came up to 87.34% in last month. It was concluded that the samples were not considerably affected at 40°C±2°C/ 75% RH ±5% RH and released the medicament in sustained form.

Second choice of drug in present study was celecoxib. Standard calibration curves for celecoxib were formulated and sketched out. It was found that the graph was linear in between absorbance and concentration and obeyed Beer Lambert law.

The celecoxib powder was found to be white off colored and free from any notable odor. The drug showed solubility in organic solvents and solublized in ethanol and methanol. For the celecoxib medicament the bulk density was viewed to be 0.55gm/ml. In same way the celecoxib medicament demonstrated tapped density of 0.42gm/ml. The Carr’s index for the celecoxib powder was found as 14.12%. From the readings of Carr’s index it was concluded that powder showed good flow property. The powder depicted 1.19 Hausner’s ratio and exhibited good flow
property. It was observed from the melting point study that compound was closely melted at the same stated temperature of 157-158°C and hence it was proved that the drug was pure.

The % moisture content for all the formulated batches was present in limit of 2.10% - 2.90%. Batch AF7 showed least amount of % moisture content i.e. 2.10% and batch AF4 depicted maximum amount of % moisture content i.e. 2.90%. All prepared batches were dried in an oven at the temperature of 110 ± 5°C till the batches reached to the constant weight gain. It was observed that all the batches of pellets has acceptable limit of moisture content. When observed by sieving method the formulated pellets were detected in 694-716 microns size range. The friability of pellets was identified less than 0.5 % and no broken pieces or particles of pellets were seen after the completion of test and hence it was concluded that pellets bear the acceptable mechanical strength and absorbed the shocks occurred during handling and transportation. It was seen that in limit of 0.71 gm/ml - 0.81 gm/ml the bulk density was exhibited by the manufactured batches of pellets. Batch AF3 showed the least bulk density among the prepared batches i.e. 0.71 gm/ml. Batch AF5 and AF 11 showed highest bulk density among all the formulated batches i.e. 0.81 gm/ml. It was declared from bulk density study that all the pellets of prepared batches showed bulk density less than 1gm/ml. Tapped density was successfully examined and finding of the study showed that it was present in the level of 0.80 gm/ml to 0.86 gm/ml for all manufactured pellets batches. The batches AF1 and AF9 showed 0.80 gm/ml of tapped density and it was the least found tapped density among all batches. The batches AF3 and AF5 illustrated 0.86 gm/ml of tapped density and it was the largest tapped density among all formulated batches.

The findings for the angle of repose showed that it was present in between 9.44° to 11.48°. As pellets of all the batches has repose angle less than 20° hence all of them showed excellent flow characteristic. It was seen form the table that less the value of angle of repose excellent was the flow property of pellets. Due to smooth and even shape surfaces of pellets the value for angle of repose was found to be low.

The percent loading of medicament over the pellets was checked by spectrophotometerically at 254nm. The drug loading for celecoxib medicament was present between 19.06 mg% to 20.98 mg %. Batch AF4 illustrated 20.98mg % drug loading where as batch AF9 showed 19.07mg% drug loading. The dissolution apparatus II of USP was employed to conduct the dissolution study and it was seen that batch AF1 released highest quantity of medicament and batch AF15
removed minimum amount of medicament in 12 hr of study. It happened due to the fact that batch AF1 contains less Eudragit RL 100 and batch AF15 contain more quantity of Eudragit RL 100. The study was performed in triplicate style and batch AF4 released 91.33 % of medicament in 12 hr. As the released pattern of batch AF4 was best suited to the present designed research work and hence was optimized.

In SEM study it was seen that all the pellets has smooth surfaces with free from cavities and deformities. No roughness was seen on their surfaces. SEM also showed that uniform coating over the pellets surfaces. No interactions of medicament and used polymers detected in IR findings. Hence it was proved that the composition was stable and suitable for administration through orally. From the Table of interpretation it was cleared that all the important and essential sharp peaks were viewed in the sample pellets. Examination of different types of liquids, solids with the help of infrared absorption spectroscopy could be done. The area used by the FTIR is from 4000 to 400 $^{-1}$. So many inorganic and organic materials showed absorption radiation in this limit of 4000 to 400 $^{-1}$. The FTIR instrument has very large accuracy in case of wave number. The chances of errors with the instrument were very rare and negligible i.e. ± 0.01cm$^{-1}$.

In was seen in DSC study that the eudragit RS 100 material gave peak at 217.98$^{0}$C. Same way eudragit RL 100 illustrated peak at 263.78$^{0}$C. It was clearly seen from the thermogram of pure celecoxib medicament that it was melted at the 163.54 $^{0}$C.The standard melting point for celecoxib mentioned within the literature is 157$^{0}$C-158$^{0}$C. The formulated pellets of celecoxib illustrated endothermic peak at 160.16 $^{0}$C which was near equivalent to the pure drug melting point. After doing comparison it was seen that the celecoxib medicament in pellets having coat of eudragit RS 100 and eudragit RL 100 was not diverged from standard melting point of medicament as mentioned in literature. Another very sharp peak which was observed in formulation thermogram at 220.51$^{0}$C was of eudragit RS100. It was also marked from the thermogram of final preparation that the actual endothermic peak of celecoxib pellets at 160.16 $^{0}$C was not very sharp. It was concluded that the celecoxib medicament was not reacted with the added material of formulation. Hence the preparation of celecoxib pellets was said to be stable.

Metals like Graphite, alumina, copper and platinum was used for the construction of pans. The pans were selected accordingly to keep away from cross reaction among pan and sample. The nitrogen gas was blown on the sample to be examined to generate dry and reproducible environment. Due to presence of nitrogen gas the chances of oxidation of material was reduced.
The apparatus which was employed in doing the current DSC work was Mettler Toledo, Germany.

The basic requirement which should be present in DSC apparatus is that it should be capable to assess the slight variation in temperature by maintaining stable rate of heating and cooling. The apparatus must performed perfect temperature examination. It was also essential that the machine should perfectly observe the variation in flow of heat among the reference and sample so as to obtain good base line with reduction in noise. Nowadays completely automatic machines are available in market equipped with devices which clean and load the material and wok in relation with the computer to load the sample. Cleaning and degassing of sample was also to be performed with the help of computer. The machine is competent enough to heat the material up to 600\(^0\) C and hence sample might be decomposed during heating process. Due to decomposition of material there might be release of harmful gases may takes place. Proper arrangement should be made for the emission of dangerous gases. It was advisable that material never be heated more than their temperature of decomposition. Before doing actual DSC work material must be dried and clean perfectly to obtained accurate and sharp peaks. Forceps was used to add the material in pan and to put the pan lid on sample. The pans must be clean and dry properly to avoid the cross contamination. If by default contamination was happened then it defiantly affects the accuracy of results. Preparation of sample a critical and most important step in DSC and hence material must be loaded very curiously inside the pan with the help of forceps only. Before going to actual experiment both the pan were checked for remained solvents and moisture of last reading. Heaters were observed to check whether they are providing heat to the reference and material equally. Speed of heating and cooling must be examined perfectly. The selection of quantity of material must be done properly and higher amount should not be added in to the pan. The whole operation must be examined keenly to avoid errors occurred during processing. During addition of material in a pan it was good to keep it thinner and it should not be compressed. Cutting of sample was good practice to gain sample having thin size.

In to the various existing kinetic models the dissolution readings were added. The model of zero order kinetic study illustrated 0.962 reading and 0.975 for Higuchi model. The Hixon Crowel model illustrated 0.972. The value showed by the Korsmeyer Peppas model was 0.966. In zero order kinetics there was fixed rate of process and it was not depend on amount of medicament taking part in the process. In first order kinetics the process has direct relation with the amount of
medicament. It was confirmed from model fitting study that batch AF4 follow first order release with highest 0.989 kinetic value as compared to other models. In first order kinetics the speed of process linearly enhanced with the enhancement in amount of medicament and the process was depend on amount of medicament.

The empty hard gelatin capsules were filled by mixing the measured quantity of medicament containing pellets with talc as lubricant and Avicel PH101 as diluent. Capsules of 00 sizes were selected for filling the content and weighed before and after filling. Care should be taken while filling the capsule to maintain uniformity of weight. The final weight of the capsules was kept at 540mg. Evaluation test was conducted on the filled capsules for checking their general appearance. It was found that all the capsules have good transparent appearance with smooth and fine texture. Neither deformities nor pinholes found on the surfaces of capsules. The batch AF4 was the optimized batch of capsules and showed 98.09% active ingredient. To attain the accurate and perfect possible results the evaluations was repeated for thrice. The weight variation test was performed on selected 20 capsules. It was found that from the average weight no capsule was deviated by higher than 7.5%. It was also seen that no single capsule was diverged by higher than two times from the same percentage limit. It was found that all the selected capsules passed the test for weight variation. All the selected capsules meet the specification as given in Indian Pharmacopoeia and passed the content uniformity test for capsules. It was viewed that there was good drug uniformity in all the ten capsules and uniform drug content was detected in all of them. The dissolution apparatus II of USP was utilized to conduct the dissolution study. The optimized batch of pellets after filling in capsules released 91.34 % of cumulative medicament in 12 hr.

The stability study on formulated capsules was successfully conducted at 40°C±2°C/ 75% RH±5% RH up to three months. Stability study revealed that appearance and texture of all the capsules were satisfactory and fine. No deformities and pinholes were noticed on the surfaces of capsules. The drug content of capsules which was 98.09 % at beginning of the study was detected up to 94.11% at the end of 3rd month after keeping them at 40°C± 2°C/ 75% RH±5% RH. In the last third month of study the obtained results proved that all capsules showed the adequate content of medicament. After every month on the optimized batch of capsules the dissolution study was performed up to three months. The percent cumulative removal of medicament was found to be 89.23% at the end of first month. At the end of second month it was
detected at 88.65% and came up to 87.37% in last month. It was declared that samples were not majorly affected by keeping them at $40^\circ C \pm 2^\circ C/75\% \text{ RH} \pm 5\% \text{ RH}$.

The last drug of preference for current study was aceclofenac. Standard calibration curves for aceclofenac were prepared and plotted by using pH1.2 and pH 7.2 phosphate buffers. Graph found to be linear in between concentration and absorbance and follow Beer Lambert law. The preformulation study on physical appearance of aceclofenac medicament was conducted and revealed that drug was white colored powder. It also seen that the aceclofenac medicament was free from any kind of smell. The drug proved solubility in organic solvents like ethanol and methanol. The bulk density found to be 0.62gm/ml. The aceclofenac showed 0.80 gm/ml of tapped density. For the aceclofenac medicament 14.80 Carr’s index was identified. Carr’s index readings showed a good flow feature in a powder. The powder showed 1.18 Hausner’s ratio and possessed good flow property. It was observed from the melting point study that compound was exactly melted at the same stated temperature of 149-153 $^\circ C$ and hence it was concluded that drug was pure.

The study of % moisture content determination was performed on all the prepared batches and it was obtained in limit of 2.11 % -2.43%. Batch AF6 demonstrated minimum quantity of % moisture content i.e. 2.11% and batch AF7 depicted largest amount of % moisture content i.e. 2.43%. All the prepared batches were dried in an oven at the temperature of $110 \pm 5^\circ C$ till the batches reached to the constant weight gain. It was achieved that in all batches of pellets acceptable limit of moisture content was present.

The formulated pellets were found to be in limit of 708-725 micron size. It observed that sieve analysis was simple and economical method and performed easily in laboratory. It was found that sieve method showed rapid and reproducible results.

After performing bulk density study it was seen that the prepared pellets batches illustrated bulk density the limit of 0.71 gm/ml to 0.80 gm/ml. The minimum 0.71 gm/ml bulk density was observed with batch AF2 among all the prepared batches. Bulk density of 0.80 gm/ml was showed by batches AF1 and AF11, it was the largest recorded bulk density among all the formulated batches. It was concluded from bulk density study that all the pellets of prepared batches showed bulk density less than 1gm/ml. The experiment will not be conducted till the glass measuring cylinder get washed twice perfectly and dried to reduce the chances of any
possible contamination with the material to be examined. If the cylinder was not clean then the adhered particles in the inside surface of cylinder may get mixed with the actual material.

It was identified that tapped density of all the formulated batches of pellets was present in limit of 0.80 gm/ml to 0.86 gm/ml. The batch AF2 and AF12 has 0.80 gm/ml of tapped density and it was least tapped density among all the batches. The batch AF1 has 0.86 gm/ml of tapped density and it was the highest tapped density among all developed batches. The result for the angle of repose presented in between 9.25° to 11.58°. It was detected that repose angle for all developed batches was less than 20° and hence all of them has excellent flow characteristic. It was also marked during study that the pellets flow feature was detected to be excellent if repose angle value is lesser. Less reading of angle of repose was attained by the pellets due to their smooth and even shape surfaces. The friability for all batches of pellets was identified to be less than 1%.

At the end of test no broken particles or pieces of pellets were observed and hence declared that pellets possessed sufficient mechanical strength and bear easily the different shocks occurred in handling and transportation. The percent loading of drug over the surfaces of pellets was evaluated by spectrophotometrically at 275 nm. The drug loading was detected between 19.27 mg% to 21.22 mg%. Batch AF5 showed the 21.22% drug loading whereas batch AF2 depicted 19.27% medicament loading.

The dissolution study revealed that quantity of released medicament decreased from batch AF1 to batch AF15. The batch AF1 has small amount of eudragit RL 100 while batch AF15 contains highest amount of eudragit RL 100. The study performed in triplicate style and batch AF5 released 92.34% medicament in 12 hr of dissolution work. It was also observed that released pattern of batch AF5 best suited to the present designed research work and hence declared optimized one. In SEM study it was viewed that all pellets has smooth surfaces. It was also examined during the study that the pellets have no deformities and cavities over their surfaces. All the pellets observed spherical in shapes. SEM also depicted uniform coating over pellets surfaces. In FTIR study no interaction was marked in between the medicament and polymers. From the Table of interpretation it was cleared that all the important and essential sharp peaks were viewed in the sample pellets.

The apparatus which was employed in doing the DSC work was Mettler Toledo, Germany. It was seen in DSC examination that the eudragit RL 100 exhibited peak at 263.78°C and eudragit RS 100 material gave peak at 217.98°C. It was clearly observed from the thermogram of pure
aceclofenac medicament that it was melted at the 153.68 °C. The standard melting point for aceclofenac mentioned inside the literature is 149°C-153°C. The formulated pellets of aceclofenac depicted endothermic peak at 160.34 °C which was near equivalent to the pure drug melting point. In comparative study it was seen that the aceclofenac medicament in pellets having eudragit RS 100 and eudragit RL 100 coat was not diverged from standard melting point of medicament as mentioned in literature. Another very sharp curve peak which was found in formulation thermogram at 220.90°C was of eudragit RS100. It was concluded that the aceclofenac medicament was not reacted with the added material of formulation. Hence the preparation of aceclofenac pellets was said to be stable. The nitrogen gas was blown on the sample to be examined to generate dry and reproducible environment. Due to presence of nitrogen gas the chances of oxidation of material was reduced. Depending up on the various functions and material to be examined the DSC are now available in various designs. The basic requirement which should be present in DSC apparatus is that it should be capable to assess the slight variation in temperature by maintaining stable rate of heating and cooling. The apparatus must performed perfect temperature examination. It was also essential that the machine should perfectly observe the variation in flow of heat among the reference and sample so as to obtain good base line with reduction in noise. It was advisable that material never be heated more than their temperature of decomposition. It was marked that at room temperature the liquid nitrogen starts to boil and hence wearing of gloves, shoes and goggle was highly advisable. Before doing actual DSC work material must be dried and clean perfectly to obtained accurate and sharp peaks. Forceps was used to add the material in pan and to put the pan lid on sample. Calibration should be conducted to get the best possible results. The pans must be clean and dry properly to avoid the cross contamination. Before going to actual experiment both the pan were checked for remained solvents and moisture of last reading. Heaters were observed to check whether they are providing heat to the reference and material equally. The selection of quantity of material must be done properly and higher amount should not be added in to the pan. The whole operation must be examined cautiously to avoid errors occurred during processing. The material should be kept thinner while its addition in a pan and it should not be compressed. It was nice to cut the material to achieve sample having thin size.

In to the various kinetic models the obtained dissolution readings were added. The model of zero order kinetic study showed 0.954 reading and 0.961 for Higuchi model. The Hixon Crowel
model illustrated value of 0.955. The value showed by the Korsmeyer Peppas model was to be 0.961. In zero order kinetics there was fixed rate of process and it was not depend on amount of medicament taking part in the process. In first order kinetics the process has direct relation with the amount of medicament. It was confirmed from model fitting study that batch AF5 follow first order release having highest 0.978 kinetic value as compared to other models. In first order kinetics the speed of process linearly enhanced with the enhancement in amount of medicament and the process was depend on amount of medicament.

The weighed quantity of pellets containing medicament mixed with diluent i.e. Avicel PH101 and talc. After suitable mixing the empty hard gelatin capsules were filled up. It was essential that the laboratory motor must be washed with water and cleaned properly before the start of experiment. Capsules of 00 sizes were selected for filling the material and weighed before and after filling. Care should be taken while filling the capsule to maintain uniformity of weight. The final weight of the capsules was kept at 540mg. The filled capsules were evaluated for general appearance. It was identified that all capsules were smooth and found with fine texture and good transparent appearance. No deformities and pinholes marked on surfaces of capsules.

The content of drug in optimized batch of capsules was found to be 98.15%. The study was performed in triplicate manner for achieving the best possible results. The weight variation test was performed on 20 capsules. It was found that from the average weight, no capsule was deviated by higher than 7.5%. It was also seen that no single capsule was diverged by higher than two times from the same percentage limit. It was declared that all capsules passed the test of weight variation. It was seen that all the ten selected capsules were meet the specification as given in Indian Pharmacopoeia and passed the content uniformity test for them. There was good drug uniformity in all the ten capsules and uniform drug content was detected in all of them. The Dissolution apparatus II of USP was employed to execute the dissolution study. It was detected that the optimized batch of pellets after filling in capsules liberated 93.39 % of cumulative medicament in 12 hr. The stability study on the formulated capsules was successfully conducted at 40°C± 2°C/ 75%RH±5% RH up to three months.

The capsules were evaluated for pinholes, deformities, texture and appearance after every month up to three months. After three months of stability study it was found that appearance and texture of all the capsules were satisfactory and fine. Neither deformities nor pinholes found over their surfaces. The drug content of capsules of AF5 batch, detected up to 94.10% at the end of 3rd
month which was 98.15% at the beginning of the study, after keeping them at 40°C±2°C/ 75% RH±5% RH. The obtained results proved that all the capsules showed adequate content of medicament at the end of 3rd month. The in vitro dissolution study carried out after every month on the optimized batch of capsules up to the three months. The percent cumulative removal of medicament was found to be 89.19% at the end of the first month. At the end of second month it was detected to be 88.36% and came up to 86.12 % in last month. It was declared that samples were not affected by keeping them at 40°C± 2°C/ 75% RH ±5% RH.

It was also viewed that increased in quantity of Eudragit RL 100 decreased the quantity of liberation of medicament. To an extent it was desirable but if the quantity of Eudragit RL 100 enhanced more than required limit then it retarded the liberation of medicament through the system. First order release rate obtained from the pellets by using Eudragit RL 100 as a sustaining agent and dibutyl phthalate as a plasticizer in proportionate quantity. All three drugs selected for the study were sustained the rate of release for the desired time being period if proper quantity of Eudragit RL 100 was used. For higher production yield the process parameters need to be optimized. The gun containing the coating solution must be properly moved on bed of pellets so as to avoid the localized wetting of pellets. Coating of pellets must be done as per the furnished details otherwise the pellets of low quality grade formed.

It was concluded that OD dose of capsule containing sustained release pellets of medicament for the treatment of arthritis was successfully prepared by the method utilized in this work. It was also gained that in current study the method used was inexpensive and for the industrial purpose it could be scale up.