CHAPTER-3

REVIEW OF LITERATURE

Akala EO, Adedoyn A and Ogunbona FA\textsuperscript{38} have formulated suppositories of antimalarial amodiaquine using PEG, glycerogelatin, whitepsol, theobroma oil and shea butter. The release of amodiaquine was more from PEG as compared to whitepsol and cocoa butter.

Allen LV\textsuperscript{39} have presented an overview of the preparation of rectal, vaginal and urethral suppositories, types of suppository bases, physicochemical considerations rates of drug release, stability, incompatibilities of various drugs with different bases.

Asikoglu M, Erton G, Cosar G\textsuperscript{40} have reported the dissolution rate of isoconazole nitrate from various suppository vehicles (Polyethylene Glycol- 6000, Polyethylene Glycol-4000, Polyethylene Glycol- 1500, whitepsol H15, Novata BD (cremao). Release rate was high with PEG 6000 when compared to that of other bases.

Axel S\textsuperscript{41} et al investigated the solid reversed micellar solution (SRMS) based suppositories of metoclopramide. The SRMS is composed of 70% witepsol W35 and 30% w/w lecithin in 1% w/w metoclopramide. The liquid crystal identified by polarized light microscopy for its lamellar mesophase. SRMS suppositories follows zero order kinetics and were sustained release in action as compared to the commercial Gastrosil suppositories. The invivo studies shows five times longer mean residence time in comparison to the commercial brand.

Basavaraj BV et al\textsuperscript{42} studied muco adhesive effect of carbopol on dissolution rate from bilayered suppositories of propranolol hydrochloride and found that by varying the carbopol concentration the release rate was increased along with drug absorption through rectal mucosa.
Brummer J.M\textsuperscript{43} et al studied that the release of cisapride was retarded when administered in the form of suppository, the impact of rectal dose on retarding the gastric emptying rate of cisapride has been studied\textsuperscript{40}. This study showed that a unit dose of cisapride 60 mg considerably accelerates gastric removing of the solid phase of a meal and radio-opaque markers in patients with previously demonstrated delayed gastric emptying.

Cyprian\textsuperscript{44} et al. It is believed that some drugs which has poor bioavailability profile such as chloroquine needs absorption enhancers for better permeation. A absorption enhancing agents could be a nonionic surfactants with sodium salicylate combination (75:25\%). Without incorporation of enhancing agents the drug release from the control formulations was 88\%, while addition of any of the three nonionic surfactants such as Tween 20, tween 80 or the Brij 35 showed complete drug release. but tween 20 was found to be more impressive than that of Brij 35 or the Tween 20. Concentration of twens plays a crucial role in drug release. Sodium salicylate has a critical concentration above which drug release rate was found to get decrease. He found 25\% w/w of sodium salicylate as an affect concentration to improve the drug release rate. Combination of tween 20 and sodium salicylate did not showed significant improvement in the release rate as compared to that of single agent. Finally, suggest that incorporation of either 4\% tween 20 & / or 25 percent weight/weight Na-salicylate is sufficient to improve drug release from the polyethylene glycol chloroquine suppositories formulations.

Dash AK, Cudworth GC\textsuperscript{45}. have evaluated an acetic acid ester of monoglyceride made from palatable oil, entirely hydrogenated (AC-70) as suppository base and distiguished it with a commonly available semi-synthetic bases.
El Assasy, The release behavior and bioavailability of pirprofen from various suppository vehicles was reported\textsuperscript{46}. The release rate was found to be in order as follows PEG > suppocire NA 10> cocoa butter > novata BD> whitepsol H15> suppocire CM> whitepsol E-75.

El-Bary AA, et al\textsuperscript{47} have studied the influence of chemical structure on the liberation of various propionic acid derivatives from different dosage forms (capsules, suppositories and creams).

E.I Taha\textsuperscript{48} and his team prepared rectal suppositories of salbutamol sulfate utilizing different bases viz., Suppocire NA, Witepsol H15, Witepsol W25 along with additives such as eudispers gel (6%) and methyl cellulose gel (3%). The bioavailability of rectal suppositories was compared with oral bioavailability by administering suppositories rectally in six healthy male.

Eva Kalmar\textsuperscript{49} et al Studied the HPLC method for analysis of drug sample from the suppository base containing 95% hard fat and tweens. It is believed that the non ionic surfactants present within the suppository base didn’t causes the significant drug release from the suppository bases. He suggested the surfactant content to be selected on the bases of turbidimetric method. This turbidimetric method of the CMC didn’t causes the degradation during drug release studies. The optimum conditions for drug release from the suppository bases was found to be 100mM Nacl, 20-40 mM NaOH and a 30 min of ultrasonic treatment of the sample solution. Degradation studies were also performed with NMR studies which was found to be absent under such harsh conditions.

Faruk Ahmed\textsuperscript{50} and coworkers investigated the effect of suppository bases and release modifiers on in-vitro release of TSG. The investigational results depicted that the drug release is significantly low from beeswax, carnauba wax. Incorporation of release modifiers such as
Polyethylene Glycol -1500 in beeswax, carnauba wax and stearic acid base suppositories increases the dissolution rate. Further inclusion of HPMC 15cps in PEG-4000 loaded suppositories rate of TSG release was faster.

Fontan et al. To enhance the dissolution rate of carbamazepine suppositories four varying surfactants were studied based on their physicochemical properties. The selected surfactants were polyoxyethylene 50 stearate, Polyoxyethylene 23 luryl ether, polysorbats 20 & 80. With 2% polysorbate 80 concentration the dissolution rate was found be enhance from 54% to 100%. However the liquification time is one of the major rate limiting factor.

Ghorab D et al., studied the effect of hydrophilic bases vs the fatty bases by preparing the fenoterol HBr suppositories. Hydrophilic bases selected were PEG and poloxamer, while fatty base selected were witepsol H-15, E-75, Suppocere AP & B.M grades. Higher release rate were obtained with hydrophilic bases in comparison to the fatty bases. Among the fatty bases witepsol H15 (F17) showed faster drug release rate. The F17 formula was subjected to the invivo studies among guinea pigs. During 30 min of studies no dyspnea was recorded. The 15% poloxmer 188 with 25 percent poloxamer 407 illustrated minimum gelation at body temperature. They concluded with suggestion that for faster release hydrophilic bases can be selected, while if sustained release is desired then fatty bases can appropriate selected for preparing suppositories.

Han et al selected that thermosensitive polymer poloxamer 407 and poloxamer 188 (15:15%) along with other additives to prepare suppositories. He studied the effect of various additives over different suppositories parameters. The additives Nacl, NaHPO4 and sodium monohydrogen phosphate tends to increases the gelling capacity and mucoadhesive force. Glycerin tends to decrease the gelation temperature, increases the gel strength. The ethanol, PG and Hcl increases the gelation temperature, but decrease the gel strength and bioadhesive force.
Author suggest that the physicochemical properties of liquid suppository bases depends upon the bonding capacities, which could be higher with Nacl, sodium mono hydrogen phosphate and NaHPO4. While weaker bonding was observed with ethanol, propylene glycol and Hcl. Overall a unique combination is necessary to obtain the desired properties of suppositories.

Hanaee J\textsuperscript{54} studied the effect of ionic and nonionic surfactant concentration namely SLS & Tween80, Arlacil 60 over the liberation kinetics of salbutamol suppository. There results illustrated that 2% tween-80 and 0.75% weight/weight SLS causes increase in the dissolution of salbutamol from these suppository. It is known that anionic surfactants such as SLS, tends to causes greater damage over the rectal mucosa as compared to tween80. Author suggest the addition of tween80 is necessary to increase the dissolution rate of salbutamol drug from the suppositories formulations.

Hender T, Hender J, Gellin F, Haung ML, Vande PS, Woestenborghs R et al\textsuperscript{55} studied the relative bioavailability of cisapride 30mg suppository and 3 5mg oral tablet and reported that the bioavailability of the cisapride from suppositories was 43\% more than that of the tablet.

Hideo S\textsuperscript{56} and co workers has developed a modern chronotherapeutic pharmaceutical formulation as SR Suppository for preventing and healing activity against asthma in the morning hours. They have prepared SR- Hollow type (HT) suppository by utilizing Na-Alginate, Na-Polyacrylate as gel forming agents. They investigated the pharmaceutical characteristics of the prepared formulations. In their investigations they have concluded that the modern formulation of SR-suppositories for chronotherapy of theophylline utilizing fatty base blend with polymers such as NA-palyacrylate co polymer. The HT suppositories comprising of fatty base and water soluble polymer in the structure may be a favourable device as suppository for rectal route of administration for achieving prolonged plasma concentration.
Hudson K C, Asbill C S, Webster A A\textsuperscript{57} studied the release of Isoniazid from selected bases such as cocoa butter, Witepsol H15 Base F, and a combination of PEG-3350, 1000 and 400 and found that the isoniazid release from hydrophilic base was more than that from the oil-soluble bases (cocoa butter and Witepsol H-15).

Iwata M et al\textsuperscript{58} Reported that delivery of diclofenac sodium from suppository including various concentrations of both witepsol W35 and witepsol E85, found that the area under the drug release curve increased and mean drug release time decreased with increased concentration of witepsol W-35 in diclofenac suppositories.

Jawahar N et al\textsuperscript{59} worked on the preparation of controlled release rectal suppository of nimesulide by utilizing fusion method using polymers such as agar, PEG 6000 and sodium-carboxymethylcellulose. The suppositories prepared using Agar (4%), PEG 6000 (4%) and sodium carboxymethyl cellulose (1.5%) showed maximum drug release.

Kamlinder KS, Deshpande SG and Biachwal MR\textsuperscript{60} have designed and evaluated suppositories using hydrophilic polymers such as sodium-CMC and agar. The study suggested that the suppositories do not melt or dissolve in body fluid, but remain intact. Drug release was modified by the use of propylene glycol, PVP and triethanolamine.

Kirsti G\textsuperscript{61} et al. In order to obtain a correction between the invitro dissolution and plasma concentration for paracetamol suppositories a analysis performed using flow through cell. The invivo study was also used to influence the statistical moment analysis and the convolution/deconvolution data based on invivo and invitro dissolution results. The optimal flow rate was found to be 28 ml/min, which readily correlates.

Md Khamaruzzaman A\textsuperscript{62} has formulated acetaminophen loaded suppositories by pour molding utilizing Polyethylene Glycol -4000 and Polyethylene Glycol -1500 and studied the
effects of viscosity enhancing polymers on dissolution rate. The study reveals that the release rate decreases as the concentration of xanthan gum and sodium CMC increase but however the release rate increases by increasing the concentration of HPMC in dissolution medium.

Kim JY and Ku YS\textsuperscript{63} studied improved bioavailability of indomethacin(IDCN) post oral and suppositories of self-emulsifying system INDCN in rat. Their study demonstrated that the presence of self-emulsifying system (30 percent weight/weight tween-85 and 70 percent weight/weight ethyl oleate) enhanced the oral absorption of the drug by 57% and rectal absorption by 41%.

L Ozguney, L Ozcan, G Ertan and T Guneri\textsuperscript{64} has prepared and evaluated sustained release suppositories of Ketoprofen using eudragit and Polyethylene Glycol of various grades and in various concentrations, and also prepared conventional suppositories using Witepsols (H-15), Massa Estarnum B, cremao in combination of polyethylene Glycol 400:6000. The delivery of drug demonstrated the sustained release of the drug for upto 8 hrs.

Lintz W et al\textsuperscript{65} have studied pharmacokinetics and bioavailability of tramadol hydrochloride in the form of suppositories, the results showed that after rectal delivery of tramadol, the sorption was rapid enough for therapeutic purpose and the extent of absolute bioavailability is higher than oral administration.

Malladi SP, Shastry et al\textsuperscript{66} have studied the stability of fast and slow release compressed propranolol hydrochloride suppositories at normal and accelerated temperature.

Maitani Y\textsuperscript{67} and his team studied the drug release of progesterone from suppositories consisting of various grades of solid fat viz., witepsol W-35 and witepsol E-85 and proposed that the suppositories prepared utilizing witepsol W-35 and Witepsol E-85(1:1) has high physical
value and the maximum temperature of the formulations illustrated a bias to elevate with increasing in the ratio of witepsol E-85. Finally he suggested that the release of progesterone from a suppository consisting of progesterone, via matrix and pores can be formulated.

Margarit \textsuperscript{68} et al. Author initially carried out the preformulation studies to determine the influence of active ingredients and adjuvants over the melting characteristics and rheological performance before formulating the suppositories. The preformulation studies were carried out using DSC and rheological studies. The excipients and the formulations follow Newtonian fluids law and there was influence of the ethosuximide drug with formulation, which was noted by increase in the viscosity of the suppository mass.

Medina JR \textsuperscript{69} et al, carried out the invitro dissolution studies on the prepared ketoprofen suppositories under hydrodynamic environment using USP apparatus 1 and 4. Their results showed poor dissolution, when USP basket was used it showed less than 10\% while better results were obtained with USP apparatus 4. Further the kinetics showed a great variability with USP apparatus 1. The author concluded with the proper need to establish an adequate dissolution method to evaluate kinetics of ketoprofen suppositories.

Mohamed RA \textsuperscript{70} et al, 2014 formulated and characterized the metoclopramide solid lipid nanoparticles, and incorporated it into the suppository bases for the remedy of revulsion using one dose per day. The solid lipid nanoparticles were prepared using different types of surfactants (tween 80, cremophore, poloxamer 407 and 188), in various concentration 2.5 \% & 5\% respectively. The poloxamer 407 based F9 formulation showed highest invitro drug release of 80\%. TEM analysis showed nanoparticles were spherical in shape and were in the size range of 24.99-396.8nm. Invivo study produces the same \% of Gastric Emptying as that of the marketed
metoclopramide suppository with sustained effect and it is considered to be suppository with no multiple dosing required.

Nair L and Bhargava HN\textsuperscript{71} have compared the dissolution and diffusion of fluconazole from four different types of suppository bases like hydrophilic (PEG), lipophilic (cocoa butter, whitepsol 45 and amphiphilic (suppocire AP)) and the found the that the release of fluconazole from various bases was in the following order PEG> (SAP=W45)>CB.

Nilufer T\textsuperscript{72} prepare the sustained release rectal suppositories of ketoprofen using chitosan along with different molecular weight PEG effect and the prepared suppositories were compared with that conventional form and predicted that the sustained release from chitosan suppository was observed .They also suggested that the drug liberation can also be altered by changing the drug:polymer concentration. The bioavailability studies were carried out in rabbit for both the prepared and conventional suppositories it was found that the drug plasma concentration was achieved in one 1hr for the forms with sustained slow rate of release and longer residence time in the rectum. Finally they concluded that the prepared suppositories reduce the rectal bioavailability by 40 % in consideration with conventional formulation.

Nishimura S, Katsunori\textsuperscript{73} and others had made an attempt to enhance the dissolution rate of nifedipine (NP) from witepsol H15, glycerine and Polyethylene Glycol suppository bases by complexing with hydroxyl propyl \( \beta \) cyclo dextrins (HP- \( \beta \)-CyD) and showed that the release of NP from witepsol H15 and glycerine were prominently improved by complexing with HP- \( \beta \) cyclo dextrins.

Pandit JK, Choudhary PK and Mishra B\textsuperscript{74} have studied the dissolution rate of pentazocine suppositories using various concentrations of PEG bases. The \textit{in vitro} release was highest in combination of 80% PEG 1000 and 20% of PEG 4000.
Pasztor E\textsuperscript{75} and his team prepared thermo reversible gelling suppositories of piroxicam using metolose which have reversible thermal gelation temperature at $68^\circ$C with an objective to reduce the thermal gelation temperature in equilibrium with body temperature for in situ gelation of liquid suppository. The thermal gelation temperature of various metalose types were studied using rotoviscometer. They studied the effect of pH and concentration on thermal gelation temperature of metalose decreases the thermal gelation temperature of metalose where as the change in pH has no effect on effect on the gelation temperature. Further they used various additives to lower the gelation temperature to body temperature was decreased using water soluble salts such as NaCl, KCl, NaHCO$_3$ and Na$_2$HPO$_4$ in varying concentrations. They concluded that 5% N Na$_2$HPO$_4$, 9% NaHCO$_3$, 10% 5KCL and 8% NaCl were able to ensure gelling at the body temperature.

Rama Rao P et al\textsuperscript{76} formulated PEG based diltiazem suppositories and compared the relative bioavailability of the drug after oral and rectal administration. The absorption rate of diltiazem was about 75% more on administering rectally when compared to that of oral route, hence, concluded that systemic effect of liver, intestine and lungs can be avoided by administering the diltiazem as a rectal suppository.

Realdon N. etal\textsuperscript{77} prepared suppositories utilizing polyethylene glycol and investigated the result of PEG on the drug release of insoluble drug and reported that the solubility was increased and the suppositories showed faster drug release from PEG suppository.

Regdon G, Schrim S\textsuperscript{78} have formulated and evaluated chloroquine suppository by using PEGs and other bases. The study revealed that PEG mixture was found as good base for suppository formulation and was stable.
Reiko Y\textsuperscript{79} et al objective were to target lidocaine absorption only from the lower rectum region. With the unique combination of witepsol H15 base, carbopol 934P and whitebeeswax additives, they formulated a mucoadhesive lidocaine suppositories. The suppositories formulation containing 10\% CP & 20\% wax remained within the lower rectum of rats for at least 2 hrs. He prepared single and double phased suppositories. The analysis illustrated that double phased mucoadhesive suppositories initially repress the lidocaine metabolism, and thereby indicates suitability to improve bioavailability of lidocaine which undergoes first pass metabolism.

Rishiraj C, Harsha B.Patel, Rajan DS, Jayanthi C, Suresh B\textsuperscript{80} Formulated and studied \textit{in vitro} characterization of chloroquine phosphate suppositories and the displacement values of the drug with different bases were calculated, the prepared suppositories were evaluated and reported that the suppositories prepared with theobroma oil and PEG has shown faster drug release.

Ryu Jm etal\textsuperscript{81}, prepared liquid suppositories of propranolol using thermally gelling suppository base and the affect of mucoadhesive agent on the bioavailability of the drug was performed. The study indicated that rectal bioavailability was increased as mucoadhesive force increased.

S Maity, B.Sa, A K Bandyopadhay\textsuperscript{82}. Prepared theophylline loaded conventional suppository, sustained release and sustained release two layered suppositories using PEG-4000 and eudragit RS-100, and evaluated their characteristics both dissolution and absorption , the dissolution of theophylline from SR suppositories was gradual and extended over a period of time and from SR two layered suppository produced an initial quick release followed by extended release of the drug . The \textit{in-vivo} results were found to correlate the \textit{in-vitro} results.
Sastri MS et al\textsuperscript{83} studied the pharmacokinetic and pharmacodynamic performance of matrix based slow release propranolol hydrochloride suppositories in rabbits and reported that the maximum relative bioavailability of propranolol from suppositories was 87.8%. About 40-50 percent of the $\beta$-blockade during 1 to 9 hours after-administration was observed and stated that better correlation between pharmacokinetic and pharmacodynamic performances was observed.

Schmitt and Guentert TW\textsuperscript{84} have shown the effect of the hydrophilic nature of suppositories bases (massa estarinum) on rectal sorption of carprofen, a lipophilic NSAID.

Schneeweis A\textsuperscript{85} and his team has investigated solid-reversed-micellar-solution drug delivery systems comprising of seventy percent witepsol w35 and thirty percent of lecithin in which one percent weight/weight of metoclopramide-HCL was incorporated. The results suggested that the solid-reversed-micellar-solution suppository gives an suitable route of controlled release of metaclopramide-HCL suppository.

Stanislaw J\textsuperscript{86}. The dissolution profile always that to vary among different marketed brands. Author selected four marketed brands A, B, C & D and modified the diffusion cell. The reproducibility of results were only observed for A & C brands. A brand showed slow release within 6 h, while suppository B brand did not softens at 37$^\circ$ C and not more than 5 percent of drug was liberated. However after melting faster release rate was reported. The results demonstrated that complete melting of the suppository base is deemed necessary to obtained dissolution of paracetamol invitro.

T A Adegboyen, O Itiola\textsuperscript{87} prepared metronidazole suppository using witepsol H15 & E75, polyethylene glycol- 2850 and 4650 bases employing various combinations of tweens, salicylates of sodium and methyl cellulose as promoting agents and the result of promoting
agents on the release characteristics of metronidazole suppository formulations was performed and showed that tween-80 and sodium salicylate may be utilized to prepare fast dissolving suppositories while methylcellulose can be used to obtain sustained release suppository.

Takatori et al. prepared the SR suppositories of using hard fats viz., polyglycerol ester of fatty acid or bees wax along with a fatty suppository vehicle witepsol H15. The inclusion of polyglycerol ester to witepsol enhanced the apparent viscosity of suppository vehicle at 37°C with no change in the melting point of the witepsol and stated that the release of acetaminophen from the prepared suppositories was delayed by inclusion of polyglycerol esters or beeswax. And hence concluded that the hard fats can manage the drug liberation from the mixed base suppositories by varying their viscosity.

Taneja LN and Jaiswal SB have investigated the bioavailability of insulin suppositories in rabbits. Examinations, were conducted to determine the effect of surface active agents to enhance insulin absorption.

Tatsumi A, Oda S, Nakamoto T, Muraoka R, Takahashi V, Tanaka k and coworkers prepared suppositories of predinosolone using powdered tablet along with witepsol H15 and E75 as suppository base by fusion method. The release study was carried out using reciprocating dialysis tube method with throbing and dialysis tubing method. The result of release test by RDT and DT method were same. Dissolution rate of predinosolone suppositories containing powdered tablet and witepsol H15 and E75 has shown good dissolution rate.

Tina K et al. has undertaken the work of manufacturing, developing and optimizing a promising pediatric suppository of azithromycin as a substitute to the existing oral or per oral drug delivery systems. They analyzed the absorption of drug and optimize solid solution of
suppository to rectal solution and intra-venous product. And depicted that the absorption of azithromycin inserted as solid solution suppositories relative to intra-venous was 43 percent when analyzed with the oral route.

Tokiko oribe\textsuperscript{92}, and his co-workers formulated lemilidipne solid-dispersion fused suppositories by employing fusion method and studied in in-vitro in-vivo correlation. They prepared lemilidipine solid dispersion using HPMC covering and organic drug-polymer solution using fluidized bed granulator. They showed that lemilidipine suppositories were more stable in oleaginous bases. The bioavailability of solid-dispersion suppository. The in vivo absorption curves of solid dispersion fused and bulk intact suppositories were obtained showing in-vivo absorption preceded at a reducing rate and the absorption rate achieved an constant level of 3\% for intact suppositories and 42 \% for solid dispersion incorporated suppositories after 12 hrs of administration. The IVIVC was correlated meaningfully.

Uzunkaya G and Bergiadi\textsuperscript{93} reported \textit{in vitro} drug liberation characteristics of controlled release indomethacin suppository, in this study, suppositories containing ethyl cellulose microcapsules of indomethacin in PEG and witepsol H-15 bases were formulated and evaluated for \textit{in vitro} drug liberation. The results illustrated that sustained effect suppositories of indomethacin has shown a sustained release upto 480 minutes.

Watanabe K\textsuperscript{94} has formulated delayed release hydrogel rectal formulation of indomethacin with hydrophilic dietary fibres, xanthan gum and locust bean gum as suppository base for rectal delivery. The peak plasma levels of the prepared suppositories were compared to that of the commercial suppositories. The commercial suppositories showed peak plasma level after 30 minutes while as prepared hydrogel suppositories has not shown any sharp plasma levels however he found that hydrogel suppositories containing one percent (Weight/Volume) gum
concentration was prolonged than those after dosing with the conventional suppositories. The overall results indicated that the indomethacin hydrogel suppositories designed with xanthan gum and locust bean gum were rectal preparation with sustained action and minimized side effects.

Young CS et al reported improved rectal absorption of ibuprofen in rats by using poloxamer-188 and menthol\(^9\). This analysis revealed that menthol enhances the rate of liberation, rectal absorption of ibuprofen from poloxamer gels.

Yuan Y\(^96\) and his team has developed and investigated thermo-labile and muco-adhesive rectal formulations of nimesulide by incorporating materials which sticks to the mucous membrane, such as Na-Alginate and thermo-labile gelling solution of polaxamer 407 and PEG’s to alter the gelation temperature and release characteristics. They investigated that gelation temperature was enhanced by the addition of addition of nimesulide to the gelation solution while addition of Na-Alginate has the reverse effect and the incorporation of PEG’s has enhanced the gelation temperature and the dissolution rate of nimesulide. They concluded that the formulation prepared with polaxamer 407-nimesulide-PEG-4000 in the following ratios 18/2/0.5/1.2 has reveals the suitable gelation temperature, satisfactory dissolution rate and rectal holding at the site of insertion.

Zia H\(^97\) et al, studies the suppositories release mechanism using different suppositories. The drug selected were a combination of ketorolac tromethamine with ketoprofen. There release kinetics suggest that a blend of release mechanisms, melting of base, succeed by partitioning along with diffusion of drug from the bases of the dissolution media. The complete bioavability of suppository preparation with ketorolac tromethamine in cocoa butter bases was shown to be sixty one percent. The release rate for various bases were found to be in the order of cococa.
better > witepsol H15 greater han witepsol w25 > suppocire AML > witepsol W35 > Hydrokote AP5-1 > witepsol E75. When the drug was formulated alone ketorolac tromethamine demonstrated faster release profile in comparison to that for ketoprofen formulations, thereby suggesting nature of the drug also affects the drug release profile.