Review of Literature:

Akala EO et al., (1991)\textsuperscript{[7]} formulated suppositories of antimalarial drug 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 (1997)\textsuperscript{[8]} 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, et al., (1996)\textsuperscript{[9]} have examined the \textit{in vitro} release of isoconazole nitrate from different suppository bases (PEG 6000, PEG 4000, PEG 1500, whitepsol H15, Novata BD (cremao). Release rate was in the following order PEG 6000 > PEG 4000 > PEG 1500 >> whitepsol H15 > cremao > novata BD.

Basavaraj BV et al., (2007)\textsuperscript{[10]} have studied the mucoadhesive effect of carbopol on drug release rate from double phased suppositories of propranolol hydrochloride was reported by. The results suggest that double phased suppositories with varied carbopol concentration can produce rectal stagnation and moderate drug release facilitating drug absorption in the lower rectum. This approach is highly beneficial for enhancing the bioavailability of drugs undergoing extensive first pass metabolism.

Brummer J.M et al., (1997)\textsuperscript{[11]} studied the effect of rectal dose of cisapride on delayed gastric emptying has been studied\textsuperscript{11}. This study showed that a single suppository dose of cisapride 60 mg significantly accelerates gastric emptying of the solid phase of a meal and radio-opaque markers in patients with previously demonstrated delayed gastric emptying.

Dash AK and Cudworth GC (2001)\textsuperscript{[12]} have evaluated an acetic acid ester of monoglyceride made from edible oil, fully hydrogenated (AC-70) as suppository base and compared it with a commercially available semisynthetic base.

El Assasy et al., (1995)\textsuperscript{[13]}, reported the release characteristics and bioavailability of pirprofen from different suppository bases. 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., (1998)** [14]. have studied the effect of chemical structure on the release of certain propionic acid derivatives from different dosage forms (capsules, suppositories and creams).

**E.I Taha et al., (2004)** [15] had prepared rectal suppositories of salbutamol sulfate utilizing various bases such as Suppocire NA, Witepsol H15, Witepsol W25 along with additives such as eudispert 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 participants.

**Faruk Ahmed et al., (2004)** [16] prepared lipid based suppositories of theophylline sodium glycinate (TSG) and investigated the effect of suppository bases and release modifiers on in-vitro release of TSG. The investigational results showed that the release rate is considerably slow from beeswax, carnauba wax acid. Incorporation of release modifiers such as PEG-1500 in beeswax, carnauba wax and stearic acid bases suppositories increased the release rate. Further inclusion of HPMC 15cps in PEG-4000 loaded suppositories rate of TSG release was faster.

**Hender T et al., (1990)** [17] studied the comparative bioavailability of cisapride 30 mg suppository and three 5mg oral tablet. This work indicated that the relative bioavailability of the drug from suppository was 43% of that of the tablet.

**Hudson Kristofer C et al., (2007)** [18]. studied the release of Isoniazid from selected bases such as cocoa butter, Witepsol H15 Base F, and a combination of polyethylene glycols 3350, 1000 and 400 and found that the drug release from water-soluble base (mixed polyethylene glycols) was significantly greater than that from the lipophilic bases (cocoa butter and Witepsol H15).

**Iwata M et al.,(1998)** [19] reported *In vitro* release of diclofenac sodium from suppositories containing different concentrations of both witepsol W-35 and witepsol E-85 and the physicochemical properties of the diclofenac sodium suppository formulations has been reported [19]. The results showed that the area under the drug release curve increased and mean drug release time decreased with increased concentration of witepsol W-35 in the diclofenac suppositories.

**Jawahar N et al., (2005)** [20], worked on the design and evaluation of sustained release suppositories of nimesulide has been reported. The unconventional, non-melting, non-
disintegrating suppositories were prepared by fusion method using polymers such as agar, PEG 6000 and sodium-carboxymethylcellulose. Agar (4%), PEG 6000 (4%) and sodium carboxymethyl cellulose (1.5%) showed maximum drug release (93.69%) by concentration independent manner.

Kamlinder KS et al., (1994)\[21\] 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.

Md Khamaruzzaman A et al., (2005)\[22\] has formulated acetaminophen loaded suppositories by fusion method using PEG-4000 and PEG-1500 and studied the effect of viscosity imparting agents on drug release. 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 (2000)\[23\] Enhanced absorption of indomethacin after oral or rectal administration of self-emulsifying system containing indomethacin to rats. Their study demonstrated that the presence of self emulsifying system (30% w/w Tween-85 and 70% w/w ethyl oleate) enhanced the oral absorption of the drug by 57% and rectal absorption by 41%.

Ozguney L et al., (2007)\[24\] has prepared and evaluated sustained release suppositories of Ketoprofen using eudragit and PEG of various grades and in various concentrations, and also prepared conventional suppositories using Witepsol H-15, Massa Estarinum B, cremao and mixture of PEG 400:6000. the dissolution studies was carried out using phosphate buffer (pH 7.2) at 50 rpm using USPXXIII basket apparatus and dissolution time was sustained upto 8 hrs.

Lintz W et al.,(1998)\[25\] have studied pharmacokinetics and bioavailability of tramadol hydrochloride in the form of suppositories, the results showed that after rectal administration of tramadol suppositories, the absorption was rapid enough for therapeutic purpose and the extent of absolute bioavailability is higher than oral administration.
Malladi SP et al., (1992) have studied the stability of fast and slow release compressed propranolol hydrochloride suppositories at room temperature and at accelerated temperature (37º).

Nair L and Bhargava HN(1999) have compared the in vitro release and permeation of fluconazole from four different types of suppository bases – hydrophilic (PEG), lipophilic (cocoa butter), whitepsol 45 and amphiphilic (suppocire AP). The order of in vitro release of fluconazole from the bases was as follows: PEG> (SAP=W45)>CB.

Nishimura K et al.,(2006) and others had made an attempt to improve the release property of nifedipine (NP) from witepsol H-15, glycerine and PEG suppository bases by complexing with hydroxyl propyl β cyclo dextrins (HP- β-CyD) and showed that the release rate of NP from witepsol H-15 and glycerine were significantly increase by complexing with HP- β-CyD.

Pandit JK et al., (1990) have studied the in vitro release of pentazocine suppositories using different combinations of PEG bases. The in vitro release was highest in combination of 80% PEG 1000 and 20% of PEG 4000.

Rama Rao P et al., (1998) formulated PEG based diltiazem suppositories and compared the relative bioavailability of the drug after oral and rectal administration. The relative bioavailability of diltiazem hydrochloride was about 75% greater after rectal administration compared to the oral route, hence, concluded that biotransformation of diltiazem by liver, intestine and lungs can be avoided by administering the drug as a rectal suppository.

Realdon N et al., (2001) studied the effect of drug solubility on the in vitro availability rate from suppositories with polyethylene glycol excipients has been studied. Factors involved in the availability mechanism of different drugs from suppositories with PEG were examined using an in vitro model of the rectal compartment with a porous membrane simulating the rectal barrier. Drugs less soluble in water showed a greater availability from PEG suppositories.

Regdon G and Schrim S (1995) have formulated and evaluated chloroquine suppository by using PEGs and other bases. The study revealed that PEG mixture was found as good base and was stable.
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Rishiraj C et al., (1999) formulated and studied in vitro characterization of chloroquine phosphate suppositories has been reported. The displacement values of the drug with different bases were determined, medicated suppositories were prepared and evaluated for pharmacopoeial specifications. Theobroma oil, PEG suppositories complied with the requirements, but later base provided a better dissolution performance (with minimum 70% in the first hour).

Ryu Jm et al., (1999) prepared Liquid suppositories of propranolol using thermally gelling suppository base and the effect of mucoadhesive polymer on the bioavailability of the drug was studied. The study indicated that rectal bioavailability was increased as mucoadhesive force increased.

S Maity et al., (2008) 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 in- vitro and in-vivo, the release of theophylline from SR matrix 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 in-vivo results were found to correlate the in-vitro results.

Sastri MS et al., (1993) 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%. There has been minimum of about 40-50% of the β-blockade during 1-9 hours post-administration and stated that good correlation between pharmacokinetic and pharmacodynamic performances was observed.

Schmitt and Guentert TW (1990) have shown the influence of the hydrophilicity of suppository bases (massa estarinum) on rectal absorption of carprofen, a lipophilic NSAID.
T A Adegboye and O Itiola(2008)\textsuperscript{[39]} prepared metronidazole suppository using witepsol (H15 and E75) and polyethylene glycol (PEG 2850 and 4650) bases using different concentrations of Tween 80, sodium salicylate and methyl cellulose as adjuvants and the effect of adjuvants on the physical and release properties of metronidazole suppositories was studied and showed that Tween 80 and sodium salicylate can be probably be used to formulate only immediate release suppositories while methylcellulose can be useful for SR metronidazole suppository.

Taneja LN et al.,(1981)\textsuperscript{[40]} 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 et al.,(2008)\textsuperscript{[41]} prepared suppositories of predinosolone using powder of pulverized tablet as raw material along with witepsol H-15 and witepsol E-75 as suppository base by fusion method. The release study was carried out using reciprocating dialysis tube method with tapping (RDT Method) and dialysis tubing method (DT Method) . The result of release test by RDT and DT method were similar. Release rate of predinosolone from the suppositories consisting of pulverized tablet and witepsol H-15 and witepsol E-75 corresponded well.

Uzunkaya G and Bergiadi(2003)\textsuperscript{[42]} reported \textit{in vitro} drug liberation and kinetics of sustained 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 release. Comparative results of SR suppositories with that of the conventional ones showed that the former has sustained effect up to 480 minutes \textit{in vitro}.

Young CS et al.,(2004)\textsuperscript{[43]} reported enhanced rectal bioavailability of ibuprofen in rats by poloxamer 188 and menthol. This study showed that menthol improved the dissolution rates, rectal bioavailability of ibuprofen from poloxamer gels.