2.0 REVIEW OF LITERATURE

Suppositories which are designed to melt at the physiological temperature compare to oral administration the rectal or vaginal drug delivery has gain importance therapeutically by avoiding the first pass metabolism. Suppositories are semisolid dosage form; they induce local effect after insertion into the body cavities. Suppositories offers many advantages a) the portal circulation is bypassed prevent first pass metabolism b) drug irritating in gastric mucosa can be given in this manner c) the influence of gastric pH and enzymatic juices can be avoided d) it can administered to patients who cannot or will not swallow e) absorption of rectum will be more rapid and more regular than from stomach or intestine f) duration of action can be prolonged, with few of disadvantages a) patient acceptability b) limited knowledge mechanism.

The focus of this thesis was to develop the drug delivery system of nanoparticle loaded suppositories of Acetyl salicylic acid (ASA) for rectal administration.

The present chapter consists of a comprehensive review of literature for a) Nanoparticles b) Reported works chitosan and other bio polymers c) Applications in drug delivery d) Suppositories types and usages d) Reported works on suppositories e) Different bases and compositions used in reported works f) Identifying drug release mechanisms g) Parameters for the evaluation of nanoparticles and suppositories.
Jesper Legarth et al., (1987) had worked on “Prostaglandin E, vaginal suppository for induction of labour: an efficient, safe and popular method” and concluded that Vaginal suppositories containing 2.5 mg PGE, constitute an effective, safe and popular method for induction of labour in patients with a favourable cervical score\(^1\).

T.W. Hermann et al., (1995) had worked on “Recent research on bioavailability of drugs from suppositories” and concluded that there is no doubt that suppositories are used in the treatment of many diseases in contemporary medicine. A remarkable number of drugs is formulated in the form of suppositories to produce either local or systemic effects. The former effect is developed by local anaesthetics, antihaemorrhoidal, vermifugal and laxative agents. The latter effect is produced mainly by analgesic, antipyretic, antihypertensive, anti-asthmatic, antimicrobial, anti-inflammatory and antineoplastic drugs administered per rectum. The elimination of drugs subject to the first-pass effects in liver and/or in the gastrointestinal tract may be partially avoided by rectal administration. Many researchers have concentrated their efforts in rectal drug absorption on those drugs which currently must be injected parenterally, e.g., antibiotics and polypeptides. The suppository may be useful as a sustained-release formulation for the long-term treatment of chronic diseases like essential hypertension, asthma, diabetes, AIDS, anaemia, etc. It is also administered in unconscious and paediatric patients as well as for the treatment of pregnancy-, chemotherapy- and allergy-induced emesis\(^2\).

E.A. Hosny et al., (1995) had worked on “Bioavailability of sustained release indomethacin suppositories containing polycarbophil” and concluded that addition of polycarbophil to polyethylene glycol suppositories results in an improvement of
bioavailability. Also, as the concentration increased from 5 to 8% a sustained blood level for at least 12 h was achieved. The key step in formulation of these suppositories is to use the optimum concentration of polycarbophil, which achieves an improvement in blood levels, sustaining action and bioavailability. Higher concentrations of polycarbophil improve sustaining action but decrease blood levels and bioavailability, whereas lower concentrations improve blood levels and bioavailability but do not significantly improve the sustaining effect 3.

T. Oribe et al., (1995) had worked on “Formulation and in-vivo, in-vitro correlation of the dissolution property of lemildipine solid dispersions-incorporated suppositories” and concluded that Lemildipine was stable in an oleaginous suppository when incorporated as a solid dispersion form, and such physical characteristics as hardness, melting point and softening time of the suppository were satisfactory for practical use. The in-vitro dissolution and in-vivo absorption of lemildipine solid dispersion incorporated oleaginous suppositories were greatly improved compared with those of intact lemildipine incorporated oleaginous suppositories. The in-vivo absorption curves were in close agreement with the in vitro dissolution curves of the corresponding suppositories generated by the modified rotating dialysis cell method equipped with a fat-treated dialysis membrane 4.

Nilfifer Tarimci et al., (1997) had worked on “Sustained release characteristics and pharmacokinetic parameters of ketoprofen suppositories using chitosan” and concluded that from the in-vitro experiments, chitosan can be considered as a suitable matrix material for sustained release suppository formulation. However, in-vivo results did not look promising. The reason is, the concentration of the polymer in a matrix type
formulation of chitosan based suppositories was the determining factor in controlling dissolution and absorption rate of the drug from the rectal mucosa. Within a few hours right after the administration of suppository into the rectum, KP was probably encapsulated in the gel matrix which was formed by chitosan granules. Therefore, the absorption rate drops down. We think that a 1:1 (drug:chitosan) containing formulation might give better bioavailability.

Cao Xuan Thanh Phuong et al., (1997) had worked on “Comparison of artemisinin suppositories, intramuscular artesunate and intravenous quinine for the treatment of severe childhood malaria” and concluded that both artemisinin suppositories and intramuscular artesunate proved safe and effective in the treatment of severe and complicated childhood malaria. The public health implications of suppository treatment of a life-threatening disease that kills millions of children in rural Africa each year are of great importance and warrant further clinical assessment of acceptability and implementation, although the possible consequences of widespread and relatively uncontrolled use of artemisinin and its derivatives also need to be assessed and taken into consideration.

H.G. Choi et al., (1998) had worked on “In situ gelling and mucoadhesive liquid suppository containing acetaminophen: enhanced bioavailability” and concluded that liquid suppository A, P 407:P 188:polycarbophil:acetaminophen 15:19:0.8:2.5%, which remained at the administered sites due to strong gel strength and mucoadhesive force, could enhance the bioavailability of acetaminophen without firstpass effect and without damaging the rectum. Furthermore, the desirable physicochemical properties such as in situ gelling property, suitable gel strength and bioadhesive force of the liquid type
suppository, could alleviate the patients a feeling of alienation, discomfort and refusal during application, increasing patient compliance\textsuperscript{7}.

Richard Koopmansl \textit{et al.}, (1998) had worked on “The pharmacokinetics of artemisinin suppositories in Vietnamese patients with malaria” and concluded that rectal administration of artemisinin probably leads to effective plasma concentrations, albeit with wide inter-individual variation. There is a need to study other rectal formulations with possibly better bioavailability, and it would be interesting to obtain pharmacokinetic data for other artemisinin derivatives after rectal administration\textsuperscript{8}.

C.O. Onyeji \textit{et al.}, (1999) had worked on “Effects of absorption enhancers in chloroquine suppository formulations: In-vitro release characteristics” and concluded that the incorporation of 4\% (w/w) Tween 20 or 25\% (w/w) sodium salicylate in the polyethylene glycol (1000:4000, 75:25\%, w/w) composite base improves the in vitro release characteristics of chloroquine from the suppository formulation. Since in vitro drug release profiles do not necessarily reflect in vivo, definitive assertion can not be made that incorporation of these adjuvants will result in enhanced bioavailability of chloroquine from the suppository formulations. However, since these adjuvants also have absorption-promoting properties, association of the improved \textit{in-vitro} release with enhanced in \textit{vivo} availability is envisaged. Thus, results of this study serve as a guide in the selection of an optimal formula regarding the type and concentrations of absorption enhancers required for optimization of chloroquine release and a possible enhancement of rectal absorption of the drug. Studies are underway to evaluate the bioavailability of chloroquine from the 25\% (w/w) sodium salicylate and/or 4\% (w/w) Tween 20-containing suppository preparations\textsuperscript{9}. 

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\textsuperscript{7} The text is presented in a readable format, ensuring that all content is clear and accurately transcribed. The page number and section title are included as per the original document's layout.
M.O.Yun et al., (1999) had worked on “Development of a thermo-reversible insulin liquid suppository with bioavailability enhancement” and concluded that Based on the results of pharmacodynamics profiles of insulin and histological assessment of the rectal tissues of rats after the dose, it is concluded that a thermo-reversible insulin liquid suppository with 10% sodium salicylate, which was easy to administer without any pain during insertion and remained at the administered site, could have potential to be developed as a more convenient, safe and effective rectal delivery system of insulin.

S.F. Ahrabi et al., (1999) had worked on “Influence of neutron activation factors on the physico–chemical properties of suppositories and their excipients” and concluded that It is possible to achieve a homogeneous distribution of radioactivity in both lipophilic and hydrophilic suppositories when applying the neutron activation technique. The physic-chemical properties of suppository excipients (PEG 300011500, 1:1, Witepsol W35 and H12) and the model drugs (Rop.HCl and 5-ASA) are maintained following 1 min of thermal neutron irradiation in a flux of 1.1-10^{13} n cm^{-2} s^{-1}. The impact of the two neutron activation factors, i.e., the incorporation of Sm2O3 and the neutron irradiation time, on the in-vitro dissolution and disintegration of the suppositories is dependent upon the physic-chemical properties and the fraction of the incorporated drug as well as the hydrophilic / lipophilic nature of the suppository base. The content of Sm_2O_3 is more critical than the neutron irradiation treatment. The chosen neutron activation conditions were those of a provocative test, i.e., the aimed g-activity was higher than necessary for a g-scintigraphic study of a rectal dosage form. Thus, a marked reduction in the amount of Sm_2O_3 without increasing the neutron irradiation dose is possible.
R. Yahagi et al., (1999) had worked on "Preparation and evaluation of double-phased mucoadhesive suppositories of lidocaine utilizing Carbopol® and white beeswax" and concluded that this double-phased suppository with both rectal stagnation and moderate drug release property facilitates drug absorption in the lower rectum effectively. This double-phased suppository may be useful for improving bioavailability of drugs with significant first-pass effect like PID12.

J Ryu et al., (1999) had worked on “Increased bioavailability of propranolol in rats by retaining thermally gelling liquid suppositories in the rectum” and concluded that for drugs that are sensitive to an extensive first-pass effect, rectal administration in the form of mucoadhesive liquid suppositories represents a promising approach for increasing the bioavailability of a drug. The increased bioavailability of acetaminophen from a polycarbophil-containing liquid suppository could also be attributed to retention of the drug at the administered site in the rectum. Sodium alginate and polycarbophil were the most effective mucoadhesive polymers for increasing the rectal bioavailability of propranolol from the poloxamer suppository. Among the mucoadhesive polymers examined, sodium alginate alone did not irritate the rectal mucosal membrane. Thus, poloxamer liquid suppositories containing sodium alginate appear to be one of the preferred formulations for these drugs13.

R. Yahagi et al., (2000) had worked on “Mucoadhesive suppositories of ramosetron hydrochloride utilizing Carbopol® “ and concluded that In absorption studies, AUC with RAM suppository containing 2% CP were 2.5 times larger than conventional H-15 suppository because of an increased release rate and a MRT prolonged by 5.8 h over the MRT of i.v. injection. Further, our antiemetic studies indicated that ramosetron
suppository containing 2% CP might have the same antiemetic effects as i.v. injections. Onset and duration of nausea induced by cytotoxic agents like cisplatin has been shown to be about 1–48 h (Triozzi and Laszlo, 1987), suggesting that 2% CP suppositories of RAM may be suitable as safe and effective antiemetic drugs, having clinical significance from a viewpoint of the patient’s quality of life.

E.M. Samy et al., (2000) had worked on “Improvement of availability of allopurinol from pharmaceutical dosage forms I- suppositories” and concluded that Co evaporation and crystallization of allopurinol in the presence of sodium salicylate exhibited an increase in the rate of drug release from different suppository bases. A greatly enhanced release rate of the drug from suppositories containing sodium salicylate produces a net increase in absorption by lowering uric acid excretion in rabbits.

Angela M. De Campos et al., (2001) developed drug delivery of cyclosporine to the ocular surface application. The major purpose of this study was to associate hydrophobic peptide with hydrophilic nanoparticles. From the results it was concluded that the prepared chitosan nanoparticles increases the contact time for the external ocular delivery. This drug delivery system was proved to be most effective in the management of keratoconjunctivitis sicca or dry eye disease.

Futoshi Shikata et al., (2002) performed a study on Bio adhesion and cellular uptake of Gadopentetic acid with naturally available gadolinium fabricated for cancer therapy. This is incorporated in chitosan nanoparticles. The results provide two key information. 1. gadolinium fabricated chitosan nanoparticles as high affinity towards the tumor cells which may be the reason for long retention of nanoparticles. 2. The injected nanoparticles containing grade 10 B that is site specific.
Tanimin Banerjee et al., (2002) Prepared and characterized ultrafine nanoparticles based on chitosan crosslinking with glutaraldehyde. The nanoparticles were prepared using reverse micelles ultrafine nanoparticles less than 100nm diameter were evaluated for various evaluation studies include particle size, FTIR (Fourier Transfer Infrared Spectroscopy) and biodistribution of nanoparticles using radiolabeling technique. The Gama-ray study displayed accumulation of nanoparticles in different regions after 30 minutes are as fallows blood (13%), liver (24%), spleen (15%), lungs. Authors concluded that the prepared nanoparticles have long circulation in blood avoiding reticuloendothelial system\textsuperscript{18}.

Yan Pan et al., (2002) Developed Bioadhesive polysaccharides for the protein delivery. The chitosan nanoparticles were developed by ionic gelation method for the delivery of insulin. The prepared nanoparticles evaluated for both \textit{in-vitro} and \textit{in-vivo} studies. Results indicate the prepared chitosan nanoparticle has excellent capacity in association and loading efficiency and insulin is active in \textit{in-vivo} conditions. From the results it was concluded that insulin loaded chitosan nanoparticles reduces the blood glucose level to normal level\textsuperscript{19}.

S. Berko´ et al., (2002) had worked on “\textit{In-vitro and in-vivo} study in rats of rectal suppositories containing furosemide” and concluded that The comparison of the membrane diffusion examinations with the actual diuretic effect shows that drug release and the pharmacological effect had the same tendency in 70\% of cases, so a greater extent of furosemide release was associated with a greater quantity of rat urine. The best results were achieved in both cases with the Suppocire AS\textsubscript{2}X base, which means that drug release was about 70\% and the animal produced about 15 ml of urine in 150 min,
and according to the literature this corresponds approximately to the daily urine quantity of a rat. The Witepsol H 15 base had better in vitro than in vivo results, while in the case of the Witepsol W 35 base the pharmacological results proved to be better than the results of the membrane diffusion examinations. This also confirms that in vivo trials are essential to get a clear picture of the drug–base–living organism interactions and thus to choose the best composition. Based on the results obtained, two compositions were found to be suitable for formulating furosemide-containing suppositories: one is the Suppocire AS₂X suppository base in itself, which proved to be the best both in the membrane diffusion and the animal experiments, and the other is the Witepsol H 15 suppository base with 1% of Cremophor RH 60 additive, which also gave optimal results with both examination methods.\textsuperscript{20}

Yongmei Xu et al., (2003) Developed chitosan nanoparticles for protein (bovine serum albumin (BSA)) delivery based on ionicgelation method. \textit{In-vitro} characterization studies (Morphology and structure characterization of nanoparticles, Determination of BSA encapsulation efficiency of nanoparticles and \textit{in-vitro} release study) were performed. It was observed from the results that altering the concentration 0.2 to 2mg/ml of BSA and chitosan 3 to 1 mg/ml enhance the encapsulation capacity, altering the molecular weight will enhance the encapsulation and drug release pattern.\textsuperscript{21}

E.S.K. Tang et al., (2003) studied the effect of ultrasonication on chitosan and chitosan nanoparticles. Ultrasonication for longer period of time decrease the mean diameter and polydispersity, zeta potential and FTIR (Fourier Transfer Infrared spectroscopy) is unaffected. Transmission electron microscopy of freshly prepared nanoparticles appears to be in spherical in shape after ultrasonication for 10 minutes
nanoparticles structure appears to be broken. Authors cautioned on excessive ultrasonication\textsuperscript{22}.

Eve Ruel-Garie´py et al., (2004) has developed thermo sensitive gels of chitosan containing hydrogel for the local delivery of paclitaxel. Novel injectable hydrogels were prepared containing medical grade chitosan and evaluated for \textit{in-vitro} release study and anti-tumor activity when exposed to \textit{in-vivo} EMT-6 murine mammary carcinoma model. The anti-tumor activity was observed between the control and test models\textsuperscript{23}.

J. Hanaee et al., (2004) had worked on “The role of various surfactants on the release of salbutamol from suppositories” and concluded that the suppositories containing Tween 80 (2\%) showed the highest MDR, followed by the formulations containing 1.5\% and 0.75\% w/w Tween 80 and SLS, respectively. Although the suppositories containing SLS produced higher dissolution rate at low concentration, suppositories containing SLS are not recommended as the best surfactant for improvement in release of salbutamol because of irritating effect of anionic surfactants on mucosa. On the other hand, the suppository formulation containing 2\% w/w of Tween 80 as non-ionic surfactant could be the best formulation in terms of producing higher dissolution rate and very low-toxicity effect on mucosa. In the case of Tween 80, a plot of the MDR (obtained based on the above equation) against the weight percentage of the surfactant in the suppository that the MDR changes linearly with the amount of Tween 80 present. The slope with correlation coefficient of 0.9897 provides a value which characterizes the effect of Tween 80 on salbutamol dissolution from suppository formulations\textsuperscript{24}.

Yan Wu et al., (2005) have prepared ammonium glycyrrhizinate chitosan nanoparticles based on ionicgelation method using pentasodiumtripolyphosphate as
crosslinking agent. Evaluated for various *in-vitro* evaluation studies (particles size, zeta potential). The major objective of the present work is to study the effect of different grades of chitosan (low molecular weight and high molecular weight chitosan) and crosslinking agent. From the results it was concluded that chitosan nanoparticles has excellent ability as carrier of ammonium glycyrrhizinate. The positive charge decreased up on encapsulation with drug. The drug release profile revealed the burst effect in the initial periods.

Zengshuan Ma *et al.*, (2005) studied the formulation factors effect (effects of cross-flow filtration on the in vivo efficacy of chitosan–insulin nanoparticles at pH 5.3 and 6.1) on chitosan insulin loaded nanoparticles on the *in-vivo* pharmacological activity. The pharmacological activity was carried out in rats and serum insulin and glucose levels were observed after the administration of fluorescein isothiocyanate. From the observation authors has expressed their opinion the formulated chitosan-insulin nanoparticles were effective in lowering the blood glucose level.

Yesim Aktas *et al.*, (2005) aimed to formulate new formulation for Z-DEVD-FMK anticaspase peptide and to utilize chitosan nanoparticles for the delivery to CNS (central nervous system). The authors concluded that the encapsulated peptide based drug delivery using chitosan nanoparticles as a promising tool for the CNS delivery.

C.S. Yong *et al.* (2005) had worked on “Physicochemical characterization and in vivo evaluation of poloxamer-based solid suppository containing diclofenac sodium in rats” and concluded that Taken together, it is concluded that the poloxamers based solid suppository composed of 97% P 124 and 3% P 188, which was a solid form at room temperature and instantly melted at physiological temperature, retained in the rectum for
at least 4 h and could not irritate or damage the rectal tissues of rats. Furthermore, the poloxamer-based suppository gave significantly higher initial plasma concentrations and faster $T_{\text{max}}$ of diclofenac sodium than did conventional PEG-based suppository, indicating that the drug from poloxamer-based suppository could be absorbed faster than that from PEG-based one in rats. Thus, the poloxamers based solid suppository with P 124 and P 188 was a mucoadhesive, safe and effective rectal dosage form for diclofenac sodium$^{28}$.

Andreas Bernkop-Schnurch et al., (2006) and his coworkers aimed to develop a novel method for the preparation of submicron particles using thiolated chitosan. Thiolated chitosan nanoparticles were developed which will substitute ionically crosslinking by covalent crosslinking, and the results indicates when compared with others. Due to their high stability due to the presence of covalent bonds, a more pronounced positive charge due to which more electrostatic interaction between particle and membrane can be expected and remaining free thiol groups, having been shown to be responsible for improved mucoadhesive and permeation enhancing properties$^{29}$.

Yaowalak Boonsongrit et al., (2006) studied on binding efficiency of high molecular weight chitosan to different drugs (Insulin, salicylic acid and diclofenac). Nanoparticles/microparticles from ionic gelation method and evaluated for different physiochemical evaluation studies. It was concluded form the results that there is no correlation between the entrapment efficiency and zeta potential. The drug release pattern is burst and independent of pH and concluded that low chitosan binding capacity to drugs cannot be used in nano/microparticles for modifying drug release$^{30}$. 
Mi LAN Kang et al., (2006) performed *in-vivo* activities of Bordetella bronchiseptica dermonecrotoksin (BBD) loaded in chitosan microspheres (CM). The present research utilized the chitosan microspheres as carriers for the immune response stimulations. The results concluded that prepared BBD-CM has a potential application in stimulating through intranasal route\(^{31}\).

Dong-Gon Kim et al., (2006) developed chitosan nanoparticles containing retinol for the application in cosmetic and pharmaceutical purpose. The prepared nanoparticles were evaluated for various evaluation studies (Particle size and zeta potential measurement, Transmission electron microscope (TEM) observation, Fourier-transform-infrared spectroscopy measurement, \(^1\)H nuclear magnetic resonance spectra study, Reconstitution test, Solubility test, High-pressure liquid chromatography (HPLC) measurement. HPLC (High Performance Liquid Chromatography) study revealed that retinol was stable and effective in encapsulating retinol\(^{32}\).

S. Itoh et al., (2006) had worked on “Reciprocating dialysis tube method: Periodic tapping improved in vitro release/dissolution testing of suppositories” and concluded that the reciprocating dialysis tube with tapping method increased the reproducibility and predictability of the release of drug from suppository base. Therefore, the reciprocating dialysis with tapping method could represent a simple and robust test for evaluating *in-vitro* release/dissolution for suppositories\(^{33}\).

Yongli Zheng et al., (2007) developed a new non stoichiometric polyelectrolyte complex using chitosan. Evaluated using various physiochemical, *in-vitro* and *in-vivo* evaluation procedures. The results shown that 5-fluro uracil chitosan polyelectrolyte
complex (5-fu, CS-PA) when compared with 5-fluro uracil solution, it was observed that 5-fu, CS-PA has shown a sustained effect, and the area under curve were increased\textsuperscript{34}.

Cinzia A. Ventura \textit{et al.}, (2007) Chitosan microspheres containing moxifloxacin for intrapulmonary drug delivery were prepared by spray drying method using glutaraldehyde as crosslinking agents. The main aim of the study is to reduce the dosage frequency. The prepared microspheres were evaluated for loading efficiency, \textit{in-vitro} drug release, Biomembrane interaction study, and intrapulmonary release study was performed using Calu-3 cell monolayer obtained from human bronchial epithelium. The results indicates moxifloxacin microspheres has prolonged drug release for four days and concluded that such a \textit{in-vivo} system will be more convincible\textsuperscript{35}.

Fu Chen \textit{et al.}, (2007) Prepared N-Trimethyl chitosan chloride nanoparticles for the delivery of bovine serum albumin and bovine hemoglobin. Evaluated for effect of physiochemical properties and \textit{in-vitro} release. Results indicate that the prepared nanoparticle has high loading efficiency of bovine serum albumin and low loading efficiency of bovine hemoglobin. With increase in particle size the zeta potential appears to be decreased. The studies demonstrated that Trim ethyl chitosan as a potential carriers and release profile can be modified using various approaches\textsuperscript{36}.

I. Bravo-Osuna \textit{et al.}, (2007) worked on cationic binding capacity of chitosan and effect of chemical modification. Authors demonstrated the chitosan containing nanoparticles are efficient in binding at much higher concentration. The results indicates the presence of positive charge is due to the thiol groups and the thiol group percentage was reduced which is useful enough to overcome the structure\textsuperscript{37}. 

\textit{Review of Literature}
Anchalee Jintapattanakit et al., (2007) Aspired to improve nanocarrier system for the delivery of insulin. Found on polyelectrolyte complexation and ionic gelation. Accompanied by TPP as counter ion for the oral delivery and to clarify the impact of TPP on colloidal solidity of insulin. The authors brief the polyelectrolyte complexation as a useful technique for the per oral administration\textsuperscript{38}.

Alexander H. Krauland et al., (2007) has developed a new type of chitosan and carboxy-β-cyclodextrin nanoparticles for the delivery of macromolecular drug delivery. Using ionic gelation method prepared nanoparticles evaluated for physiochemical characterization. The result includes zeta potential positive charge, smaller size, and greater efficiency in carrying two macromolecular drugs tested i.e. insulin and heparin. From the results it was concluded by the authors the prepared nanoparticles will provide greater scope in delivery of macromolecular drugs\textsuperscript{39}.

Waree Tiyaboonchai et al., (2007) Prepared a novel nanoparticles system for the delivery of amphotericin B using chitosan and dextran sulphate as a carriers. The nanoparticles prepared based on polyelectrolyte complex technique. The prepared nano complexes were evaluated for physiochemical properties and in-vitro drug release study. The authors conclude the particle sizes of the prepared nono complexes are in size range of 600-800nm and potential enough in use for targeted delivery. The major advantage of the used technique involves 1. Ease of preparation and simple preparation conditions 2. Use of biocompatible polymer 3. Usage aqueous solvent for the production reduces the toxicity\textsuperscript{40}.

Sanjay K. Motwani et al., (2008) has developed Chitosan–sodium alginate nanoparticles as submicroscopic reservoirs for ocular delivery. The main objective
development and optimizing the gatifloxacin for ocular drug delivery using Box-Behnken statistical design. Prepared nanoparticles were evaluated for various in-vitro evaluation studies from the results it was concluded that the new formulation developed provided a new approach for the ocular drug delivery due to the sustaining effect of gatifloxacin.

Wei Sun et al., (2008) Prepared poly electrolyte complexes (PEC) using chitosan derivatives. Enoxaparin (low molecular weight heparin) was used as a host element. The prepared PEC were characterized using particle size, zeta potential, morphology and various factors effecting PEC formation. Based on the results it was concluded that PEC formation was influenced various factors such as pH, drug : polymer ratio and the size range of soluble PEC was 200nm and spherical morphology can be obtained at pH 3 to 6.5.

A.M.M. Sadeghi et al., (2008) developed and compared the nanoparticles using quaternized derivatives of chitosan (trimethyl chitosan (TMC), dimethylethyl chitosan (DMEC), diethylmethyl chitosan (DEMC) and triethyl chitosan (TEC) containing insulin as a host. The generated Poly electrolyte complexes (PEC) compared for permeation efficiency through Caco-2 cell layer. It was concluded that for the oral delivery of hydrophilic compounds and peptides chitosan in free form is more efficient for the permeation.

Akbar Bayat et al., (2008) Prepared nanoparticles of quaternized chitosan derivatives (Chitosan, Triethylchitosan, Dimethylethylchitosan) for the delivery of insulin to the colonic site. Chitosan nanoparticles were prepared based on PEC (polyelectrolyte complex method) and evaluated for ex-vivo and in-vivo studies. From the results authors
concluded that chitosan nanoparticles as a promising vehicle for the oral administration of protein and peptide molecules via the colon route.\textsuperscript{44}

Aihua Lin \textit{et al.}, (2008) worked on surface-modified chitosan nanoparticles. Present work adriamycin was used as model drug for the targeted delivery to hepatocyte. The surface of chitosan nanoparticles was modified using Glycyrrhizin. Nanoparticles were evaluated for their morphology, particle size, zeta potential, association efficiency and \textit{in-vitro} release. From the results it was concluded that surface modified nanoparticles has potential efficiency in targeting the hepatocytes.\textsuperscript{45}

B. Sayın \textit{et al.}, (2008) developed a mucosal application for the delivery of vaccine. The main aim and objective of the study was to develop a antigen delivery system for the mucosal immunization using negatively charged (N- Carboxy methyl chitosan) and positively charged (N-Trimethyl chitosan) and compare their efficiency. The prepared nanoparticles were evaluated for both \textit{in-vitro} and \textit{in-vivo} evaluation study. Authors suggested the prepared N-carboxy methyl chitosan nanoparticles as a promising deliver for both protein and gene delivery.\textsuperscript{46}

Xu-Bo Yuan \textit{et al.}, (2008) has prepared rapamycin chitosan/polylactic acid nanoparticles. Authors investigated on immunosuppressive effect of rapamycin-chitosan nanoparticles. Chitosan/polylacticacid-rapamycin nanoparticles were prepared based on nanoprecipitation method. The residence time of nanoparticles was examined under gama scintigraphy study. From the results it was concluded by the authors that nanoparticles study showed an excellent property of immunosuppressant activity when compared with rapamycin eye drops.\textsuperscript{47}
Yu GAO et al., (2008) designed a more efficient non viral gene. Authors investigated chitosan nanoparticles for the delivery of Arginine/DNA and its transfection efficiency. The self assembled made nanoparticles evaluated for in-vitro transfection efficiency, cytotoxicity assays. The result indicates that chitosan linking with arginine with amide group enhances the water solubility and transfection efficiency\textsuperscript{48}.

Su-Jin Cheong et al., (2009) Studied iron oxide nanoparticles for imaging the target hepatocyte to aid in the treatment of various liver diseases. Iron oxide nanoparticles were prepared using conjugation method. The prepared conjugates were evaluated for various in-vivo studies. In-vivo transfection efficiency and cell uptake capacity was confirmed using radio labeling technique in rats. Authors believed that water-soluble chitosan linoleic acid nanoparticles developed has potential in targeting hepatocytes for radio imaging and effective in gene delivery\textsuperscript{49}.

Noemi Csaba et al., (2009) Prepared chitosan nanoparticles based on low molecular weight and high molecular weight chitosan using pentasodiumtripolyphosphate as crosslinking agent. The main objective of this study was to use the ionicgelation technique for the delivery of different nucleic acids, and the prepared nanoparticles were evaluated for different key parameters. Authors concluded the prepared nanoparticles are better encapsulation efficiency, sustainable in drug delivery for both other molecules and nucleic acids\textsuperscript{50}.

F.A. Oyarzun-Ampuero et al., (2009) Studied nanocarriers prepared using chitosan and hyaluronic acid for heparin delivery to pulmonary system. Nanoparticles were prepared by spontaneous based up on ionicgelation method and evaluated for both in-vitro and in-vivo study. In-vivo transfection efficiency and release study was
performed in rats using fluorescent nanoparticles study. Based on the results it was concluded that the prepared chitosan and hyaluronic acid are suitable for the treatment for asthma. From the tissue distribution study performed using confocal microscopy revealed the localization of nanoparticles in mast cells\textsuperscript{51}.

Erem Bilensoy \textit{et al.}, (2009) Prepared Intravesical cationic nanoparticles using chitosan and polycaprolactone for the Mitomycin C for the delivery to urinary bladder. The main aim and objective of the study was to develop and optimize nanoparticulate carrier using cationic polymers and evaluated for various \textit{in-vitro} characterization techniques. From the various evaluation tests conducted authors concluded that, the usage of polycaprolactone with bio adhesive polymer like chitosan for the intravesical drug delivery system results in good loading and release profile. The usage of chitosan as a coating material exhibits good cellular interaction and anti cancer efficiency. Authors planned to carry out \textit{in-vivo} behavior study in animal as feature project\textsuperscript{52}.

Noha Nafee \textit{et al.}, (2009) worked on colloidal stability of chitosan and PLGA nanoparticles on their cytotoxicity profile. The main objective of the present work carried to evaluate the cytotoxicity of prepared nanoparticles prepared nanoparticles incubated with cos-1 cells. The authors expressed their opinion Potential toxicity of chitosan nanoparticles is due to reduction in chitosan concentration, adsorption of medium components over the surface of nanoparticles which shifts the pH slightly. Which will lead to loss of structural integrity of the membrane\textsuperscript{53}.

Chang-Moon Lee \textit{et al.}, (2009) Developed Super paramagnetic iron oxide nanocrystals loaded chitosan – linoleic nanoparticles for the hepatocytes target. The main aim of the study was to develop a polymeric magnetic nano probe for the evaluation of
targeting efficiency. Initially Super paramagnetic iron oxide nanocrystals were prepared by thermal decomposition and later on incorporated in to self assembled nanoparticulate systems. The prepared nanoparticulate system was evaluated for size distribution, morphology, and cytotoxicity and other evaluation studies from the results authors came to conclusion that the developed nanoparticles has successfully localized in the leaver, and it was proved using MRI study. The authors planned to conduct their feature studies using Superparamagnetic iron oxide nanocrystals as a contrast agent to diagnose the progress of hepatic disease using cirrhosis model.

Weijia Wang et al., (2010) Fabricated biodegradable chitosan hallow nanoparticles using poly-D, L-lactidepoly (ethylene glycol) (PELA) nanoparticles. In this study chitosan was used a cytoskeleton and the prepared nanoparticles were evaluated for various in-vitro and in-vivo evaluation tests from the results authors concluded that the prepared hallow nanoparticles have greater potential in drug delivery system.

Laurence Plapied et al., (2010) Studies the non animal derivative of chitosan produced from mushroom used for characterization for the delivery of DNA. In this study authors conducted simultaneous study on chemically modified fungal chitosan. The main aim of the study is to evaluate the fungal chitosan as a non viral carrier and its influence on transfection efficiency trough M-cells. Based on the observations authors conclude that the developed fungal chitosan nanoparticles appears to promising novel carriers for the gene delivery and oral vaccination.

Siling Wang et al., (2010) N-trimethyl chitosan chloride nanoparticles for the delivery of anti-neuro excitation peptide for brain targeting. The trimethyl chitosan nanoparticles prepared by ionicgelation technique using Tripolyphosphate as crosslinking
agent. Evaluated for their properties and mechanism of targeting. The results conformed the efficiency of biodistribution of nanoparticles in to the brain. The result suggests that the prepared nanoparticles are effective tools for brain targeting\textsuperscript{57}.

Jianing Qi \textit{et al.}, (2010) designed the biocompatible bovine serum albumin (BSA)-dextran-chitosan nanoparticles based on electrostatic interaction between bovine serum albumin and chitosan. In this study doxorubicin was used as model drug. The nanoparticles were characterized for \textit{in-vitro, in-vivo} efficiency and antitumor activity of doxorubicin. From the results it was conclude that the doxorubicin loaded nanoparticles reduces the toxicity and survivability hepatoma H22 tumor bearing mice\textsuperscript{58}.

Abdallah Makhlof \textit{et al.}, (2010) has synthesized glycol chitosan-thioglycolic acid polymer conjugate and to developed nanoparticles for the pulmonary drug delivery of calcitonin. The prepared nanoparticles were evaluated for the \textit{in-vivo} mucoadhesive properties and in-vivo absorption efficiency in rats. The hypoglycemic activity was prolonged for a period of 12 to 24 h. It was concluded that the prepared nanoparticles were safe enough for the pulmonary peptide delivery\textsuperscript{59}.

Jinghua Duan \textit{et al.}, (2010) Prepared curcumin loaded chitosan/poly butyl cyanoacrylate nanoparticles for the anti-cancer treatment. The prepared nanoparticles were evaluated for both \textit{in-vitro} and \textit{in-vivo} antitumor activity against human hepatocellular carcinoma cells. From the results it was conclude that the curcumin has both direct and indirect anti-angiogenic activity. The prepared curcumin nanoparticles provide a greater opportunity in effective clinical use and greater anticancer tool\textsuperscript{60}.

Shaoling Zhang \textit{et al.}, (2010) Prepared chitosan solid nanoparticles based on one step electro spray deposition. The main objective of the present study to know the effect
of various solution properties and process parameters on electro spray behavior. Results indicate that particle size can be controlled by solution and operation parameters. Particle decreased increasing the conductivity or with a decrease in viscosity. The small size 124 nm prepared during the experiment. From the results it was concluded that electro spray method has advantage mild experimental conditions and promising method for producing micro and nanoparticles for the oral and pulmonary formulation.

Nan Zhang et al., (2010) has developed insulin controlled release nanoparticles using cationic polymer β-cyclodextrin, alginate and chitosan for sustained delivery. The authors aimed to prepare β-cyclodextrin loaded nanoparticles using alginate and chitosan as the self assemble complexes. Due to the cationic charge the nanoparticulate material will form a complex with insulin which will decrease the gastric degradation of insulin. The prepared nanoparticles were evaluated for various evaluation studies. Particle size analysis, morphology, Percentage entrapment efficiency, Percentage release, stability studies, e.t.c. From the results it was concluded that the prepared nanoparticles from two mechanisms electrostatic interaction and inclusion. The prepared nanoparticles preparation insulin was well protected from degradation and the structure of insulin was well protected during release in stimulated gastric fluids.

Sheng-hao Zhao et al., (2010) Developed chitosan nanoparticles for the delivery of the delivery of parathyroid hormone related proteins. In this present research work authors used chitosan and epoxy propyl trimethyl ammonium chloride were used to prepared N-(2-hydroxy) propyl-3-trimethyl ammonium chitosan chloride were used and sodium Tripolyphosphate was used as crosslinking agent for the preparation of nanoparticles, and evaluated for various in-vitro evaluation studies like particle size
distribution, particle morphology using transmission electron microscopy, entrapment efficiency, and in-vitro drug release. From the results authors concluded that the prepared nanoparticles are excellent in capacity of loading, and the particle are round and encapsulation efficiency of maximum 78% and initial burst release fallowed by controlled release. Authors planned to conduct further in-vivo experiments in feature since in-vitro release proved the prepared nanoparticles are efficient enough in drug delivery.

Merlin Rajam et al., (2011) Studied chitosan nanoparticles for the dual growth factor delivery system for tissue engineering application. The objective of the present work was to develop bio degradable nanoparticles for the delivery of epidermal growth factor and fibro blast growth factor. The prepared nanoparticles were evaluated for various in-vitro evaluation tests and cytotoxicity and proliferation studies were performed using fibroblast cells and inflammatory reactions were carried out using macrophages. From the results it was concluded that chitosan nanoparticles exhibit good biocompatibility and no toxicity. Attachment of growth factors were greatly improved inflammatory induction compared other groups. The study suggested the capability of unification of two growth factors for tissue engineering application.

Sudhir S. Chakravarthi et al., (2011) Developed paclitaxel nanoparticles for enhanced cellular association using chitosan and PLGA nanoparticles. The aim of the present research was to develop paclitaxel nanoparticles containing PLGA (poly lactic glycolic acid) and to evaluate. Compare the cellular association and cytotoxicity of paclitaxel when delivered through the nanoparticles. Quantification of cellular association of paclitaxel nanoparticles. To establish a correlation initial amount of chitosan and
amount of chitosan utilized in the preparations. From the results it was concluded by the authors PLGA used alters the surface charge. PLGA conjugate nanoparticles has absorption efficiency was 81% to 98%. The rate and extent of release of nanoparticles significantly did not altered by the modification of nanoparticles. The cellular association was confirmed by using the confocal microscopy for cellular association. From this authors confirmed that paclitaxel cellular association and cytotoxicity profile significantly enhances the delivery of chitosan-PLGA nanoparticles.

Azza A. Mahmoud et al., (2011) Developed chitosan/β cyclodextrin nanoparticles for the effective ocular delivery. Econazole nitrate was used as model drug. The prepared nanoparticles were optimized by studying the loading efficiency, Process yield, zeta potential, Particle size, and drug release. The selected formulation was test for in-vivo in rabbit’s eye. At the conclusion prepared nanoparticles enhanced and controlled drug at surface of rabbit’s eye and these carriers represents to be promising for the delivery of drug effectively.

<table>
<thead>
<tr>
<th>S.No</th>
<th>Author’s Name</th>
<th>Name of research work</th>
<th>Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Polatti et al., (1993)</td>
<td>Effects of salmon calcitonin suppositories In the prevention of bone loss in oophorectomized women</td>
<td>This method is faster and efficient than the USP method since the latter suffers from the formation of an emulsion that require about 8h to separate for each of the four extractions.</td>
</tr>
<tr>
<td>3</td>
<td>E.A. Hosny et al., (1995)</td>
<td>Bioavailability of sustained release Indomethacin suppositories containing polycarbophil</td>
<td>Addition of polycarbophil to polyethylene glycol suppositories results in an improvement of bioavailability. Also, as the concentration increased from 5 to 8% a sustained blood level for at least 12 h was achieved.</td>
</tr>
</tbody>
</table>

Table: 2.1 Literature reviews of suppositories

Review of Literature
<table>
<thead>
<tr>
<th></th>
<th>Authors</th>
<th>Title</th>
<th>Details</th>
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<tbody>
<tr>
<td>4</td>
<td>E.A.Hosny et al., (1996)</td>
<td>Formulation, <em>in-vitro</em> release and <em>ex-vivo</em> spasmytic effects of mebeverin hydrochloride suppositories containing polycarbophil (or) polysorbate 80</td>
<td>The addition of 1% tween 80 or 55 polycarbophil to the polyethylene glycol suppositories containing mebeverine hydrochloride is essential to improve the release and absorption of drug as a magnitude of inhibitions include by the formulations containing these two additives were comparable at both dose levels.</td>
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<tr>
<td>6</td>
<td>Ehab A. Hosny et al., (1996)</td>
<td>Effect of polycarbophil concentration on diclofeace sodium bioavailability from suppositories in beagle dogs</td>
<td>Polycarbophil as a good Bioadhesive polymer that is not absorbed does not produced any undesirable systemic effects and approved by FDA for use in humans could be used an additive in suppository formulations to increases the rate and extent of drug absorption provided that it is used in the proper concentration.</td>
</tr>
<tr>
<td>7</td>
<td>P.Fumoleau et al.,(1997)</td>
<td>Ondansetron suppository : an effective Treatment for the Prevention of Emetic Disorders Induced by Cisplatin - based Chemotherapy</td>
<td>The suppository formulation is an effective alternative to the intravenous and oral forms currently available, it is particular suitable in the outpatient and palliative care setting.</td>
</tr>
<tr>
<td>8</td>
<td>N. Tarmeci et al., (1997)</td>
<td>Sustained release characteristics and pharmacokinetic parameters of ketoprofen suppositories using chitosan</td>
<td><em>In-vitro</em> experiments, chitosan can be considered as a suitable matrix material for sustained release suppository formulation.</td>
</tr>
<tr>
<td>9</td>
<td>H.G. Choi et al., (1998)</td>
<td><em>In-situ</em> gelling and mucoadhesive liquid suppository containing acetaminophen enhanced bioavailability</td>
<td>Liquid suppository, which remains at the administered sites due to strong gel strength and mucoadhesive force, could enhance the bioavailability of acetaminophen without first pass effect and without damaging the rectum.</td>
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<tr>
<td></td>
<td>Author(s) and Year</td>
<td>Title and Details</td>
<td>Summary</td>
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<tr>
<td>10</td>
<td>Rafael A. Alomdovar et al., (1998)</td>
<td>Inverse supercritical extraction of acetaminophen from suppositories</td>
<td>A larger and longer-term studies are needed to evaluate the efficiency of the newly developed GL suppository for these patients especially for those who do not respond with viral clearance interferon therapy.</td>
</tr>
<tr>
<td>11</td>
<td>M.O. Yun et al.,(1999)</td>
<td>Development of a thermo-reversible insulin liquid suppository with bioavailability enhancement</td>
<td>It is concluded that a thermo-reversible insulin liquid suppository with 10% sodium salicylate, which was easy to administer without any pain during insertion and remained at the administered site, could have potential to be developed as a more convenient, safe and effective rectal delivery system of insulin.</td>
</tr>
<tr>
<td>12</td>
<td>R.Yahagi et al.,(1999)</td>
<td>Preparation and evaluation of double-phased mucoadhesive suppositories of lidocaine utilizing carbopol and white bees wax</td>
<td>The results suggest that this double phased suppository with both rectal stagnation and moderate drug release property facilitates drug absorption in the lower rectum effectively. This double-phased suppository may be useful for improving bioavailability of drugs with significant first-pass effect like LID.</td>
</tr>
<tr>
<td>13</td>
<td>C.O. Onyeji et al., (1999)</td>
<td>Effects of absorption enhancers in chloroquine suppository formulations: I In-vitro release characteristics</td>
<td>The results of this study serve as a guide in the selection of an optimal formula regarding the type and concentrations of absorption enhancers required for optimization of chloroquine release and a possible enhancement of rectal absorption of the drug. Studies are underway to evaluate the bioavailability.</td>
</tr>
<tr>
<td>14</td>
<td>E.M.Samy et al., (2000)</td>
<td>Improvement of availability of allopurinol from pharmaceutical dosage forms – suppositories</td>
<td>Co-evaporation and crystallization of allopurinol in the presence of sodium salicylate exhibited an increase in the rate of drug release from different suppository bases.</td>
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<tr>
<td>15</td>
<td>R. Yahagi et al. (2000)</td>
<td>Mucoadhesive suppositories of ramosetron hydrochloride utilizing Carbopol®</td>
<td>Absorption studies, AUC with RAM suppository containing 2% CP were 2.5 times larger than conventional H-15 suppository because of an increased release rate and a MRT prolonged by 5.8 h over the MRT of i.v injection.</td>
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<td>No.</td>
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<td>16</td>
<td>F.K.Glowka et al., (2000)</td>
<td>Stereo selective pharmacokinetics of ibuprofen and its Lysinate from suppositories in rabbits</td>
<td>The extent of IBP ionization has failed to significantly affect the rate of its chiral inversion, lysinate or acidic form, its R(-) enantiomer has been eliminated faster than S(-) enantiomer and the difference has proven to be significant at $\alpha = 0.05$.</td>
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<td>17</td>
<td>S. Berko´ et al.,(2002)</td>
<td><em>In-vitro</em> and <em>in-vivo</em> study in rats of rectal suppositories containing furosemide</td>
<td>The pharmacological results proved to be better than the results of the membrane diffusion examinations. This also confirms that <em>in- vivo</em> trials are essential to get a clear picture of the drug-base-living organism interactions and thus to choose the best composition.</td>
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<tr>
<td>18</td>
<td>Masateru Miyake et al., (2004)</td>
<td>Development of suppositories formulation safely improving rectal absorption of rebamipide, a poorly absorbable drug, by utilizing sodium laurate and taurine</td>
<td>Present study clearly shows that the combinatorial use of C12 with Tau enables us to develop the safe suppositories formulation to improve the absorption of poorly soluble and poorly drugs such as rebamipide.</td>
</tr>
<tr>
<td>19</td>
<td>C.S. Yong et al., (2004)</td>
<td>Preparation of ibuprofen-loaded liquid suppository using eutectic mixture system with menthol</td>
<td>It is concluded that the liquid suppository system developed using eutectic mixture with menthol, which gave the improved solubility of ibuprofen, it has given significantly higher initial plasma concentrations, $C_{\text{max}}$ and AUC of ibuprofen than did solid suppository.</td>
</tr>
<tr>
<td>20</td>
<td>T.Takatori et al., (2004)</td>
<td>Evaluation of sustained release suppositories prepared with fatty base including solid fats with high melting points</td>
<td>The prepared controlled release suppositories consisting of a fatty suppository base, witepsol H15, and solid fats such as PS500, HB750 and beeswax. The addition of solid fats increased the apparent viscosity of the mixed bases at 37°C, leading to the reduction of drug diffusivity within the melted base, and the subsequent reduction of drug release rate.</td>
</tr>
<tr>
<td>21</td>
<td>J. Hanaee et al., (2004)</td>
<td>The role of various surfactants on the release of salbutamol from suppositories</td>
<td>The suppositories containing Tween 80 (2%) showed the highest MDR, followed by the formulations containing 1.5% and 0.75% w/w Tween 80 and SLS, respectively.</td>
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</table>
| 22 | E.I Taha et al., (2004) | Bioavailability assessment of a salbutamol sulfate suppositories in human volunteers | From the results authors can conclude that by adequate selection of the vehicle, the rectal bioavailability of salbutamol sulfate could be improved to match that of oral tablets. 

23 | S. Labbozetta, et al., (2005) | Focused microwave-assisted extraction and LC determination of the active ingredient in naproxen – based suppositories | The method developed generates equivalents results when compared to conventional BP method. The analytical procedure described could provide an alternative fast and accurate method or rapid screening of naproxen-based suppositories. 

24 | C.S. Young et al., (2006) | Enhanced anti-tumor activity and alleviated hepatotoxicity of clotrimazole-loaded suppository using poloxamer-propylene glycol gel | The poloxamers-based solid suppository composed of 70% P 188 and 30% propylene glycol, which was a solid form at room temperature and instantly melted at physiological temperature, could not irritate or damage the rectal tissues of rats, and gave the improved anti tumor activity and less hepatotoxicity. 

25 | Shinya Uehara et al., (2006) | A pilot study evaluating the safety and effectiveness of Lactobacillus vaginal suppositories in patients with recurrent urinary tract infection | It is recommended that future studies focus on determining the optimal dosage, duration and mode of lactobacilli delivery for establishing vaginal and/or per urethral colonization. Furthermore it is proposed that prospective randomized studies be performed. 


27 | Yu HIRABAYASHI ET AL., (2009) | Efficacy of a diazepam suppository at preventing febrile seizure recurrence during a single febrile illness | Diazepam suppository after a febrile seizure will reduce the recurrence of febrile seizures during the same febrile illness. However, a diazepam suppository after a febrile seizure should be used only after carefully considering the potential adverse effects. |
| 29  | Ravi Sankar. et al., (2012) | A Comparative Pharmacokinetic study of Aspirin Suppositories and Aspirin Nanoparticles Loaded Suppositories | ASA-nanoparticles loaded suppositories proved to be safe and effective with no observed histological changes rather than histological changes such as ulceration and necrosis due to continuous use of ASA-suppositories. |

**Conclusion**

From the above literature review it was evident that nanoparticles prepared using chitosan as polymer has number of advantages such as, site specific targeting, increases the bioavailability. Conventional suppositories suffers with disadvantages, irritation, leakage, so from the literature the idea of combination of both nanoparticles and suppositories was evolved which aimed to decrease the irritation, and ulcerative problems on continuous usage and increase the bioavailability.