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<u>Review Article</u>

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SUPPOSITORY: A REVIEW

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ABSTRACT

In ancient era, drugs inducing unconsciousness, haemorrhoedal, vermicidal and purgative actions was inserted though rectal route in the form of suppository. In modern days most of the remedial medicines are prepared for rectal delivery to gain therapeutic blood concentration of the medicine and thereby enhancing the bio-availability. By inserting the drug through rectal route the pre-systemic effect in hepatic region and in GIT can be prohibited. Anal drug delivery systems, used as controlled release dosage form for treating the ailments like arthritis, increase blood pressure, asthma, AIDS and diabetes. Moreover, there is a rising interest that the suppositories can be used in the treatment of post operative pain and pain related with malignancy. Rectal drug delivery system is the area of enthusiasm for

many researcher's to evaluate consumption of drug from the rectal region for drug which are currently inserted through parental route. Viz., antibiotic and polypeptides The absorption of antibiotic and polypeptides is more effective from the small intestine than form the rectum and hence can be formulated using different absorption enhancers.^[1]

KEYWORDS: suppository, unconsciousness, pre-systemic effect, Rectal drug delivery system, absorption enhancers

INTRODUCTION

Suppositories are solid preparations each containing one or more active ingredients and are suitable for rectal administration. They are normally intended for use as a single dose for local action or systemic absorption of the active ingredients. The active ingredients are ground and passed through a sieve, if necessary, and dissolved or dispersed in a suitable basis that may be soluble or dispersible in water or that may melt at body temperature. Suppositories may contain suitable auxiliary substances such as absorbents, dilutents, lubricants, antimicrobial preservatives and colouring agents permitted under the Drugs and Cosmetics Rules, 1945 Moulded Suppositories: Moulded Suppositories are manufactured by liquefying by heating the mass containing the medicament(s) and auxiliary substances and then pouring the mass into moulds of suitable volume and cooling in order to solidify the mass. In some cases, the solid medicated mass may be cold-moulded by compression in a suitable matrix. Moulded Suppositories have the characteristics of Moulded Pessaries. Shell Suppositories: Shell Suppositories, also known as Rectal Capsules, are generally similar to Soft Capsules except that they may have lubricating coatings. Shell Suppositories have the characteristics of Shell Pessaries.

Standards:- Moulded Suppositories and Shell Suppositories comply with the tests stated under Moulded Pessaries and Shell Pessaries respectively.^[1]

ADVANTAGES, DISADVANTAGES AND APPLICATION OF SUPPOSITORIES^[2] Advantages

a) Improved enzymatic drug stability: Many proteolytic and other enzymes in the GIT(Gastro Intestinal Tract) result in drug degradation, which prevents effective absorption following oral administration.

b) **Partial avoidance of hepatic first pass**: The rectum is extensively supplied with blood from the various rectal arteries. It is drained by at least three veins and drug absorption occurs through this venous network. It is usually reported that inferior and the inferior venacava is connected to the middle rectal veins. This allows bypassing the portal system and the associated first pass metabolism in the liver.

c) Higher drug load: Suppositories allow for two to three times higher drug loads to be administered, depending on the amounts of other excipients necessary in their formulation.

d) **Lymphatic delivery**: many researcher have studied and suggested that some of the drugs after rectal administration enters in to the lymphatic system thus bypassing the first pass effect.

e) Constant and static environment: Compared to the oral route of administration, the rectal route provides a much more constant environment for the drug as it is absorbed.

f) **Patients with swallowing difficulty**: Children, elderly people facing problems in swallowing can be largely obviated by the rectal administration.

g) **Avoidance of overdosing**: Certain drugs, viz., sedative oral administration may raise a concern with respect to the possibility of severe accidental or intentional overdosing. This danger is particularly eliminated by rectal administration.^[1]

Disadvantages

a) Patient acceptance and compliance: In many cultures reluctance to consider rectal administration as dosage form has resulted in a tendency by pharmaceutical company to avoid rectal dosage forms, except for most obvious indications and situations.

b) Potential for non-specific drug loss: Ineffective absorption due to premature loss from rectum and interaction of fecal matter with the drug or excipient may reduce absorption and diminish effectiveness.

c) **Limited fluid in rectum:** Small volume (3 ml) may limit dissolution of drug particularly with low aqueous solubility.

d) **Formulation:** Melting, liquefaction, solubility, particle size, etc. can lead to formulation difficulties.

e) Expensive: These are more expensive as compared to tablets.^[1]

Applications of Suppository

Suppositories are generally used for unconscious and pediatric patients and in geriatric persons. Suppositories are used for both systemic and local actions, where alternative routes are unavailable. A wide range of drugs have been incorporated into suppositories as shown in the following.

Different categories of drugs incorporated into suppository Drug Category Researchers Example Suppository base

1. Antibiotics: example Ceftizoxime Amoxicyllin using Thiobroma Cefmetazole

2. Analgesics: Indomethacin Paracetamol using PEG &glycero-gelatin Etodolac Ketoprofen using PEG

3. Bronchodilators/ anti-asthamatics: Theophylline Terbutaline.^[1]

MATERIALS AND METHODS

Medline (1950-2006) was searched for all published reports using the key words "Suppositories, anal, hemorrhoids, rectum and proctology". This study sum up various suppositories used in proctological practice, which either are in vogue and have been used with a proven degree of success, or suppositories which are described in the literature but are

no more in use. The study attempts to highlight the advantages and drawbacks of each of them. The suppositories used for inflammatory and irritable bowel disease, malignancy and systemic infection have been excluded.^[2]

Suppositories Containing Local Anesthetics agents

The local anesthetics act by numbing the nerve endings and provide temporary relief from pain and itching. These act by causing a reversible block to conduction in the sensory nerves. These are well absorbed from the mucus membrane and used as surface anesthetics6. These provide good relief from discomfort encountered in cases of strangulated hemorrhoids, fissures and perianal hematoms. Some commonly used local anesthetics are.

Benzocaine 5 to 20%, Lidocaine 2 to 5%, Cinchocaine, Dibucaine 0.25% to 1%, Dyclonine 0.5% to 1%, Pramoxine 1% and Tetracain 0.5 to 5%.

Suppositories Containing Steroids

Several glucocorticosteroids are used in rectal suppositories. They include hydrocortis one and its derivatives, diflucortolone valerate and prednisolone8. The steroids act as decongestant, anti-inflammatory and anti pruritic agents and in doing so they eliminate inflammation and mucus discharge. It has been postulated that the analgesic effect of the local anesthetics is apparently prolonged by an increase in the threshold for pain by the antiinflammatory effect of steroid.

Suppositories Containing Astringents

The astringent causes the cells of the anal skin to clump thereby drying the skin, which gives relief from burning and itching. Some common astringents that are used include *Hamamelis water*, which is a mild astringent prepared from twigs of *Hamamelis virginiana*. It helps in relief from the hemorrhoidal itch. Zinc oxide 5 to 25% prevents the irritation at the perianal area by forming a physical barrier on the skin that prevents the contact of the irritated skin with aggravating liquid or stool from the rectum.

Vasoconstrictors in Suppositories

Hemorrhoidal cushions contain swollen blood vessels. The vasoconstricting agents can help in relieving symptoms of hemorrhoids. On application, these drugs cause the blood vessels to shrink, thereby reducing hemorrhoidal congestion. These products additionally contain mild form of anesthetic, which helps in relieving pain and itching. The commonly used vasoconstrictors are: Ephedrine sulfate 0.1 to 1.25%, Epinephrine 0.005 to 0.01% and Phenylephrine 0.25%.

Protectants in Suppositories

Passing hard and dry stool is the most traumatic experience in patients having anal pathology as it results in tearing of the skin around the anus, as also in tearing and cracking which ends in bleeding. Again, when this tender skin comes in contact with liquid or stool, it causes the skin to further itch and burn. Protectants, when applied in the form of suppositories, form a physical barrier on the skin and results in reducing the pain quotient and the pruritus. These also protect the broken skin from coming in contact with offending particles in the stool. While a variety of protectants are used in suppositories, a few commonly used are: Aluminium hydroxide gel11, Glycerin, Lanolin, *Aloe vera*, White petrolatum, Zinc oxide and Calamine.

Use of Antiseptics in Suppositories

Being a highly contaminated area, the anal and perianal skin are susceptible to variety of organisms, which can lodge there either from the adjoining area or from the contaminated stool. The chances of contamination further increase when the skin gets bruised during defecation. Antiseptics are used to keep the area clean and to prevent infection. The commonly incorporated antiseptics include: Benzalkonium chloride, Boric acid and Framycetine sulphate.^[2]

Use of Keratolytics in Suppositories

Certain chemicals cause the outer layers of skin and other tissues to disintegrate when applied. They eventually help in better penetration in the tissues of other medications contained in the suppositories to bring quicker relief. The two commonly used keratolytics are: Aluminium chlorhydroxy allantoinate 0.2 to 2% and Resorcinol 1 to 3%. Use of Calcium Dobesilate in Suppositories Calcium dobesilate is a veno-tonic drug, which is widely prescribed for three main indications: chronic venous disease, diabetic retinopathy and the symptoms of hemorrhoidal attack. The drug acts on the endothelial layer and basement membrane of the blood capillaries. It reduces capillary hyperpermeability by increasing the activity of endothelial nitric oxide synthase in vascular endothelial cells, leading to an increase in nitric oxide synthesis. Along with Calcium dobesilate, the suppositories usually

contain local anesthetic, steroid and astringent in addition [Smuth suppositories from Aristo Pharmaceuticals, Mumbai, India].^[2]

Suppositories Containing Policresulen

Policresulen is a polymolecular organic acid. It coagulates necrotic or pathogenically altered tissue in anorectal disorder and promotes desquamation of such tissues. The healthy tissues surrounding the wound are not affected. As local hemostatic, Policresulen coagulates blood proteins thereby inducing muscle fibers of small vessels to contract and thus any hemorrhage in the anal canal or in the perianal area could be controlled. It also induces hyperemia in the wound area and thereby stimulates regeneration and re-epithelization process. It also has a antimicrobial property which guards against infection and prevents inflammation. Policresulen also has astringent property and thus it suppresses oozing.

Other Ingredients in Suppositories

Imiquimod containing suppositories have been successfully used to prevent recurrence of anal condylomata. Trimebutine, an anal sphincter relaxant, has been used to relieve post hemorrhoidectomy pain. Ketoprofen suppositories were recommended in patients after anal surgery. A sedative cryotherapy was being used with the intention of producing tissue hypothermia, giving cool numbing effect over the hemorrhoids. Promethazine suppositories were proposed for hemorrhoidal complications while trichloroacetic acid was used for the treatment of anal fissure. A compound Carraghenates suppositories has been shown to be useful in the treatment of mixed hemorrhoids. Few old references have described use of Roinal. Glycofuranoside derivatives. Indacine, Prothanon, Rhubarb and Aloe. Phenylindanedione, Proctoglivenol in suppositories form. However, they are no more in use. The various ingredients in suppositories form with their use; adverse effects.^[2]

INSERTION TECHNIQUE OF SUPPOSITORIES

It has been suggested that the suppositories should be inserted with the patient lying on the left lateral side with the right knee bent. The suppositories should be dipped in water before use, which facilitates the easy insertion of the suppositories. It should be kept in cold water or refrigerator for half an hour before use if the suppositories are too soft to be inserted, especially during warm weather. Emptying of bowel should be avoided for at least an hour after insertion of the suppositories to allow it to be fully absorbed.^[2]

METHOD OF PREPARATION

Preparation of vaginal suppositories containing L. paracasei HL32 Four formulations of L. paracasei HL32 vaginal suppositories were formulated. The compositions of these formulations are presented in Table 1. Conventional suppositories (Formulation no. 1 and 2) were prepared by fusion method. The Witepsol H-15 or mixed PEGs (blending of PEG 400 and PEG 4000 in the ratio of 1:1) as the suppository base was melted over the water bath. Then, lyophilized L. paracasei HL32 was added in the melted base at the temperature about 40-45°C with gentle stirring until a homogeneous mass was produced. The mixture was poured into a metal suppository mold at a temperature just above the congealing point of the suppository base and cooled. Hollowtype suppositories (Formulation no. 3 and 4), shown in Figure 1, were prepared by the method reported by Watanabe et al. In brief, Witepsol H-15 or mixed PEGs base was melted at approximately 40°C and 60°C, respectively, poured into the suppository mold equipped with cylindrical tube in the center of the mold and allowed to solidify for 1 hours at room temperature. After construction of a hollow cavity of the solidified base, the lyophilized L. paracasei HL32 was added to each cavity. The opening at the hind part of the suppository was sealed with the melted base. Each suppository contained 108 CFU of L. paracasei HL32. All the prepared suppositories were kept in the refrigerator for further studies.^[3]

COMPOSITIONS OF VAGINAL SUPPOSITORIES CONTAINING 108CFU OF L. PARACASEI HL32

Table No-1.

Formulation no.	Suppository base	Туре
1	Witepsol H-15	Conventional
2	Mixed PEGs	Conventional
3	Witepsol H-15	Hollow-type
4	Mixed PEGs	Hollow-type





Fig No-1: Evaluation of Physical Properties of Vaginal Suppositories.

Physical Parameters

- a) Visual Evaluation: Surface appearance and color can be verified visually to assess the absence of fissure, pit, blooming, exudates and transfer of drug.
- **b)** Melting Range : Melting range test are performed to check the physical and absorption characteristics of each manufactured batch
- c) Liquefaction Time: It detemines the period required for a suppository to liquefy under simulated conditions of rectal mucosa in presence of water at body temperature. This signifies the physical nature of suppository subjected to highest degree of temperature (37°C). Liquefaction time should be no longer than 30 minutes.
- d) Mechanical Strength: This is the determination of the mechanical force necessary to break a suppository and indicates whether a suppository is brittle or elastic. The Erweka method is used for this test. The mechanical strength in no case should be less than 1.8 to 2 Kg as measured by Erweka method. The tensile strength of suppositories is determined by hardness or breaking test. The tensile strength of suppository asses the ability of suppository to withstand hazards of packaging and transportation.^[3]

Chemical testing

Analytical Testing

Investigation of the determination of assay, content uniformity and dissolution parameters of suppository formulation.

a) Assay: Four steps are involved in the analysis of active ingredients in a unit dose formulation.

- 1) Preparation of uniform composite.
- 2) Extraction of the drug from the excipients.
- 3) Separation of excipients from the mixture
- 4) Analysis that selectively quantitates the active components.

b) Content Uniformity

The dose to dose variation can be accomplished by content uniformity in which suppository are randomly chosen to check drug content uniformity as per USP/BP specification.

c) Dissolution Testing

The in vitro assessment of product efficacy can be determined by dissolution studies.

Under FDA guidelines, dissolution testing is also a requirement for suppository to test for hardness and polymorphic changes of drug substance and base in both control and stability testing. The following methods are used in dissolution testing of suppositories.

- 1) Basket method
- 2) Paddle method
- 3) Beaker method
- 4) Diffusion method
- 5) Dialysis method
- 6) Continuous flow method.^[4]



Fig 2: Suppository penetration apparatus.

RELEASE MECHANISM

The liquefaction and softening time of suppository, dispersion of active ingredient and diffusion of drug through rectal mucosa determines the rate release and initiation of therapeutic effect. The below mentioned relationship gives a broad understanding of the relationship of how the drug is released by utilizing various suppository bases.

Relationship between drug release-drug -suppository Base.

Table No-2

Acitve ingredient (Drug)	Base Release Rate	
Oil soluble active ingredient Oily vehicle	Retarded rate of release and minimum	
On soluble active ingredient-Ony vehicle	escaping efficiency	
Hydrophilic active ingrdient -Oily base	Faster dissolution rate	
Oil soluble active ingredient – hydrophilic	optimal dissolution rate	
Base		
Hydrophilic active ingrdient - Hydrophilic	slow dissolution rate	
Base		

For hydrophilic suppositories made from PEG etc., the drug release is by dissolution and for those suppositories made from hydrogels like agar, CMC, etc, the drug release is by diffusion mechanism. For lipophilic suppositories made from cocoa butter etc., the drug release is by melting of the suppository. The release rate form the rectal suppositories can be considered as mass transport phenomenon involving diffusion of drug from a region of higher concentration in the dosage form to a region of lower concentration in the surrounding environment. Attempts to drug release from the suppositories have been reported that the mechanism follows in accordance with Higuchi's equation.

 $Q = Kt^{1/2}$

Where Q = Weight in gm of drug release

t = time Thus for diffusion controlled mechanism, a graph of cumulative percent drug released against the \sqrt{T} should be straight line (linearity). The drug release can also be confined to any other order viz., zero or first order process.

Preformulation Studies

As the physical and chemical properties changes with internal structure of the solid drug, including melting point, density, hardness, crystal shape, optical characteristics and vapour pressure, characterization of polymorphic forms and solvated forms involves quantitative analysis of these varying physical land chemical properties. Different methods for studying the solid forms are as follows.^[1]

- 1) Microscopy
- 2) Fusion Method(Hot stage Microscopy)
- 3) Differential Scaning Colorimetry (D.S.C)
- 4) I.R spectroscopy
- 5) X-Ray powder difraction
- 6) Scaning Electron Microscopy
- 7) Thermogravimetry
- 8) Dissolution or solubility evaluation

Disintegration Test

The disintegration test of lactobacillus vaginal suppositories was modified from the method described by BP [15] by using tablet disintegrator. The suppository to be tested was placed in a cylindrical glass container with perforated ends and immersed in 1,000 ml of citric acid/phosphate buffer solution pH 4.4 maintained at 37 ± 0.5 °C.The cylindrical glass container was moved up and down in the buffer. The time for disintegration was noted when the suppository has completely melted (Witepsol) or dissolved (PEG) in the medium. The mean values were calculated from six parallel measurements.

Differential Scanning Calorimetry

The thermal properties of Witepsol H-15 and mixed PEGs suppository base were studied on a differential scanning calorimeter (DSC) (Perkin-Elmer DSC7, Norwalk Connecticut, USA). Samples (6-8 mg) were accurately weighed and heated in closed aluminium crimp cells at the rate of 10°C/min under nitrogen purge with a flow rate of 35 ml/min over 20°C to 110°C temperature range.^[1]

SPECIFIC PROBLEMS IN FORMULATING SUPPOSITORIES

During the formulation of suppositories various problems arises which are as follows.

- 1) Water in suppositories
- 2) Hygroscopicity
- 3) Incompatibilities
- 4) Viscosity
- 5) Brittleness
- 6) Density
- 7) Volume contraction
- 8) Lubricant or mould release agent

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- 9) Weight and volume control
- 10) Rancidity and antioxidant.

1) Water in suppositories

The use of water should be avoided as a solvent for incorporating substances in suppository bases for the following apprehensions.

- 1) Water accelerate the oxidation of fats.
- 2) Evaporation of water causes the crystallization of dissolved substances.
- 3) If water is present at a higher concentration than that require for dissolving the drug, the water has little effect on drug absorption. The rate of absorption from suppositories containing water increases only if an oil in water emulsion exist.
- 4) The presence of water in suppository result in the possible interaction between the ingredient contained in the suppository to avoid these problems anhydrous bases are used.
- 5) Bacteriostatic agents such as parabens are incorporated in the formulation to avoid the
- 6) fungal growth and contamination.

2) Hygroscopicity

The use of hygroscopic ingredients such as glycerine and gelatin. In suppository formulation it loses moisture by evaporation in dry atmosphere and absorb moisture under condition of high humidity. Polyethylene glycols are also hyroscopic in nature but the rate of moisture change in PEG depends not only on the humidity but also chain length of the molecule, as the chain length increases the hygroscopicity decreases.

3) Incompatibilities

PEG bases are found to be incompatible with silver salts, tannic acids and sulfonamides.

Most of the chemical have the tendency to crystallize out of PEG. Higher concentration of salicylic acid softens PEG to an ointment like consistency and asprin complexs it.

4) Viscosity

In the manufacture of suppository and its behaviour in the rectal region after melting depends upon the viscosity of the suppository mass. Therefore for suppositories made with low viscosity bases extra care should be taken to avoid sedmintation of suspended particles. To avoid the segregation of particles suspended in the molten base the well mixed molten mass must be handled at the lowest temperature necessary to maintain fluidity, constantly stirred without entrapping air and quickly solidified in the mold. The given below approaches may be taken to overcome the problems caused by low viscosity base.

a) Narrow melting range bases should be used.

b) 2% aluminium, monosterate used in the formulation increases the viscosity of the fatty base, and also aids in maintaining a homogenous suspension of insoluble material.

5) Brittleness

Synthetic fatty bases which have a high degree of hydrogenation and stearate contents are brittle when compared to the cocoa butter suppositories, which are elastic in nature and do notfracture readily. Fracturing of the suppositories prepared with such bases is often induced by rapid chilling of the melted base in an extremely cold mould. To overcome the problems of fracturing and brittleness. The temperature difference among the melted base and mould should be as low as possible. The brittleness of suppositories can be avoided by using the small amount of tweens, castor oil, propylene glycol etc.

6) Density

The volume of mould cavity is fixed depending on the density of the mass. The knowledge of suppository wt can be obtained from a given mould, and density of the chosen base, the active ingredients can then be added to the bulk base, in such an amount that exact quantity of drug is present in each moulded suppositories. Density alone cannot be the criterion for the calculating suppository weight per fixed volume mould. Therefore volume contraction must be considered.^[1]

7) Volume contraction

This phenomenon occurs in many melted suppository bases after cooling in the mould. The results are described in following ways.

1) Good mould release:- This is caused by the mass pulling apart from the sides of the mould. This shrinkage facilitates the removal of suppositories from the mould eliminating the need for mould release agents.

2) Contraction hole formation at the open end of the mould. This unwanted effects results in lowered suppository weight and imperfect appearance of the suppository. This type of volume shrinkage can be avoided by draining a mass slightly over its congealing temperature into a mould heated to about same temperature. In volume production using standard mould were adequate control of temperature may not be feasible, the mould is over filled so that the excess mass containing the contraction hole can be scrapped off.

8) Lubricants or mold release agents

The suppositories from cocoa butter have a tendency to adhere to the suppository molds because of low volume contraction and is difficult to remove from the mold. Therefore various mold release as mold lubricants are used to rectify the problems of cocoa butter suppositories. The agents used are mineral oil, aqueous solution of sodium lauryl sulphate and various silicons, alcohol and tincture of green.

9) Weight and volume control

The amount of active ingredients or drug in each suppository depend on the following.

- 1. The amount of drug in the bulk
- 2. The capacity of the mold volume
- 3. The specific gravity of the base
- 4. The volume difference among he molds
- 5. Weight difference among suppositories due to improper manufacturing process.

10) Rancidity and antioxidants

Rancidity results from the anti oxidation and subsequent decomposition of unsaturated fats into low and medium molecular weight saturated and unsaturated aldehydes, ketones and acid which have stable disagreeable odors the lower content of unsaturated fatty acid constituent in the suppository base the greater the resistance to rancidity.^[1]

DISCUSSION

Drug treatment for various ano-rectal conditions has been known since ancient times. Today, modern as well as traditional drugs are being increasingly used in proctology practice. Rectal route with local or general effects is an interesting possibility of a treatment modality. Easy use and rapid absorption are two major advantages of these therapeutic options. Suppositories are a very feasible mode of administration for medication. The medicament is incorporated into a base, which either melts at body temperature or dissolves in the mucus secretions and exerts localized or systemic action. Within the era of cost-containment and the risk of AIDS and other communicable blood borne diseases, drug delivery through suppositories is proving an effective and viable option. It is well recognized that over-the-counter therapy with suppositories is an enormously large market. Suppositories are mainly used in proctology practice to produce a local action, such as anti-inflammatory and anesthetic effect for hemorrhoidal conditions. Preparations for haemorrhoids usually contain astringents, local anesthetics, veno-toner drugs and anti-inflammatory components. However, as much as

suppositories are useful, there are some disadvantages of using them too. They may not be a preferred option for the patient as it is inconvenient to use them. Absorption of drugs can be erratic and unpredictable. Some suppositories either leak or are expelled after insertion resulting in a futile exercise. Nevertheless, complications of serious nature have been reported after use of medicated suppositories. There is, thus, a need to become more creative in deciding the optimal mode of delivery of drugs to the patients. This route of drug delivery should be made more convenient in nursing facilities and institutionalized care settings. It is important to assess if the patient can self-administer a suppositories or not.

REFERENCES

- Larry JC and Herbert AL (1987), Suppositories. In: Lachman L, Liberman HA and Kanig JC. (eds.) The Theory and Practice of Industrial Pharmacy. 3rd ed. Varghese Publishing House, Mumbai, 564-587.
- P.J. GUPTA Suppositories in anal disorders: a review European Review for Medical and Pharmacological Sciences Gupta Nursing Home, Laxminagar, NAGPUR (India), 2007; 11: 165-170.
- S Kaewnopparat, and N Kaewnopparat Formulation and Evaluation of Vaginal Suppositories Containing Lactobacillus World Academy of Science, Engineering and Technology International Journal of Medical, Health, Biomedical, Bioengineering and Pharmaceutical Engineering, 2009; 3(7).
- 4. Siewert M, Dressman J, Brown CK *et al.* FIP/AAPS guidelines to dissolution/in vitro release testing of novel/special dosage forms. *AAPS Pharm Sci Tech*, 2003; 4: E7.