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Current & Practical Compounding Information for the Pharmacist.

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COMPOUNDING RECTAL DOSAGE FORMS-PART II

GOALS AND OBJECTIVES

Goal: To provide information and support on formulating suppositories including the newer unique types of suppositories reported in literature.

Objectives: After reading and studying the article, the reader will be able to:

1. List the three primary reasons for using suppositories.
2. Discuss the physicochemical factors for using suppositories.
3. List the different types of bases commonly used in suppositories.
4. Describe the newer special suppositories appearing in the research literature.

INTRODUCTION

This is the second in a two-part series on compounding rectal dosage forms. Part I discussed formulation of rectal enemas, microenemas, gels, ointments and aerosols. Part II discusses formulation of rectal suppositories with the addition of new and novel types of suppositories that can be compounded. Each part has example formulations included.

SUPPOSITORIES

Although suppositories are not very popular as a mode of administering drugs, they will probably always have a place in medicine. Suppositories have been employed for three reasons, to (1) promote defecation, (2) introduce drugs into the body, and (3) treat anorectal diseases. Suppositories are solid dosage forms intended for insertion into body orifices (rectum, vagina or urethra) where they melt, soften, or dissolve and exert localized or systemic effects.

Local Action

For local action, once a suppository is inserted, the suppository base melts, softens, or dissolves, distributing the medication it carries to the tissues of the region. Rectal suppositories intended for localized action are most frequently used to relieve constipation or pain, irritation, itching, and inflammation associated with hemorrhoids or other anorectal conditions.

Systemic Action

One contemporary question that needs to be addressed for all active drugs to be used in suppository dosage forms for systemic effects is the bioavailability of the drug. This is important so dosage adjustments can be made if necessary. Numerous orally administered drugs have relatively poor bioavailability but the dosage is adjusted so they are effective; the same situation applies with rectal or vaginal administration of suppositories. Physicians and patients usually only consider a suppository dosage form for a specific therapy if, under given conditions, the rectal pathway will allow for a satisfactory rate and extent of absorption of the active ingredients.

Anatomy of a Suppository

Suppositories generally consist of an active drug incorporated into an inert matrix, which may be either a rigid or semi-rigid base. This intimate mixture of the drug and inert matrix must be formulated to be free of any interactions between the two to avoid any alteration either of the active or the inert matrix. The inactive part of suppositories, or excipients, has a role to disperse or dilute, sometimes to protect and to allow the introduction of the active drug into the patient. After administration, the role of the suppository is to release the active principle, either by melting due to body temperature or by dissolving in the local mucosal fluids, and then to release the active ingredient so it is free to produce a local effect or to move to the mucosal barriers into the circulatory system to produce a systemic effect.

Physicochemical Factors Affecting Therapeutic Efficacy of Suppositories: Physicochemical factors of the active ingredient include such properties as the relative solubility of the drug in lipid and in water and the particle size of a dispersed drug. Physicochemical factors of the base include its ability to melt, soften, or dissolve at body temperature, its ability to release the drug substance, and its hydrophilic or hydrophobic character.

Solubility of the Active Substance: The rate at which active substances are released from a suppository and absorbed by the rectal mucous membrane is directly related to the solubility of the active substances in the excipients or, in other words, to the partition coefficient of the active substances between the excipients and the rectal liquids. Active substances which are highly soluble in the excipients in fact diffuse much less rapidly out of the excipients than do those active principles which are insoluble or have a low excipient solubility, and hence the former are not so easily absorbed. Water soluble excipients play a role above all in the rate of diffusion, the

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liquefaction rate and the high viscosity which these excipients give to the rectal liquids. It should also be mentioned that an extremely important factor is the concentration of active principles on the absorbing membranes. As in all passive absorbing processes, notably in the process of absorption of the gastric membrane, the degree of rectal absorption is directly linked to a concentration gradient, and still more important is the existence in the mucous membrane compartment (rectum) of high and rapidly reached concentration levels.

Lipid-water Solubility: The lipid-water partition coefficient of a drug is an important consideration in the selection of the suppository base and in anticipating drug release from that base. A lipophilic drug that is distributed in a fatty suppository base in low concentration has less of a tendency to escape to the surrounding aqueous fluids than would a hydrophilic substance present in a fatty base to an extent approaching its saturation. Water soluble bases-for example, polyethylene glycols-which dissolve in the anorectal fluids, release for absorption both water-soluble and oil-soluble drugs. Naturally, the more drug a base contains, the more drug will be available for potential absorption. However, if the concentration of a drug in the intestinal lumen is above a particular amount, which varies with the drug, the rate of absorption is not changed by a further increase in the concentration of the drug.

Particle Size: For drugs present in a suppository in the undissolved state, the size of the drug particle will influence its rate of dissolution and its availability for absorption. Whenever the active principle has a limited water solubility, the use of finely divided products (high specific surface area) often leads to an increase in the absorption of the drug. Here, as well as in oral medication absorption, the rate of absorption is influenced by the dissolution rate, which in turn is related to the particle size of the active principle.

Nature of the Base: As indicated earlier, the base must be capable of melting, softening, or dissolving to release its drug components for absorption. If the base interacts with the drug inhibiting its release, drug absorption will be impaired or even prevented. Also, if the base is irritating to the mucous membranes of the rectum, it may initiate a colonic response and a bowel movement, negating the prospect of complete drug release and absorption.

Spreading Capacity: It is easy to understand that the rapidity and intensity of the therapeutic effects of suppositories are very much related to the surface area of the rectal mucous membrane covered by the melted excipient:active ingredient mixture. In other words, the spreading capacity of the suppositories. This spreading capacity may be related to the presence of surfactants in the excipients.

pH, pKa and Degree of Ionization: These factors, which are physicochemical in nature may have an effect on the rate and extent of absorption. Absorption tends to increase when the degree of ionization is minimized, which can be related to the pH of the fluid in the immediate vicinity of the dosage form and the pKa of the drug. In some instances, suppositories have been proven to have better absorption than orally administered medications.

Bioequivalence: Drug absorption from rectal suppositories is a complex process of suppository melting or dissolution, movement of drug through the liquefied base to an interface where it is released, dissolved or moved into the rectal or vaginal fluids and drug permeation across the rectal or vaginal membranes. Both rectal and oral routes of administration can be bioequivalent. The rectal route, however, can even be considered as an alternative administration route for some drugs. Bioavailability of solids can be maximized by using the smallest particle size available. Also, drugs that are available as water-soluble salt forms will generally go into solution easier in the mucosal fluids, followed by migration to the rectal wall and absorption.

Choice of Drug: The first consideration in designing a suppository is the drug to be used. What are the requirements for a drug that is to be administered as a suppository? First, one must determine if it will be adequately absorbed via the rectal mucosa to obtain therapeutic blood levels. If not, can a penetration enhancer be included in the formulation to promote absorption to the desired extent?

Choice of the Suppository Base: A suppository base performs two important functions. First, it serves as a carrier for the active drug in an appropriate way considering both its physicochemical characteristics and its requirements during preparation. Second, it can be used to control delivery of the active drug at the site of absorption. It is apparent then, that selection of the base involves the nature of the active, manufacturing procedures required and the desired release characteristics of the active drug from the base. Also, the base must be non-reactive with the active, nontoxic, stable and nonirritating.

Classification of Suppository Bases: Four classifications of suppository bases are usually described. The first is the fat or oil type base which must melt at body temperature to release its medication. The second is the glycerin-gelatin base suppository which absorbs water and dissolves to release its medication. The third is the water-soluble or water miscible polymers and surface-active agents. The fourth is a group of bases containing disintegrating agents, natural gums, effervescent agents, collagen, fibrin etc.

Fatty or Oleaginous Bases: Fatty bases are perhaps the most frequently employed suppository bases, principally because cocoa butter is a member of this group of substances. Among the other fatty or oleaginous materials used in suppository bases are many hydrogenated fatty acids of vegetable oils such as palm kernel oil and cottonseed oil. Also, fat-based compounds containing compounds of glycerin with the higher molecular weight fatty acids, such as palmitic and stearic acids, may be found in fatty suppository bases. Such compounds as glyceryl monostearate and glyceryl monopalmitate are examples. In some instances, suppository bases are prepared with the fatty materials emulsified or with an emulsifying agent present to prompt emulsification when the suppository makes contact with the aqueous body fluids.

Other bases in this category include commercial products such as Fattibase™ (triglycerides from palm, palm kernel, and coconut oils with self-emulsifying glyceryl monostearate and polyoxyl stearate), the Wecobee bases (triglycerides derived from coconut oil), and the Witepsol bases (triglycerides of saturated fatty acids C12-C18 with varied portions of the corresponding partial glycerides).

Fattibase™ is a preblended suppository base that offers the advantages of a cocoa butter base with few of the drawbacks. This base is stable with a low irritation profile, needs no special storage conditions, is uniform in composition, and has a bland taste and controlled melting range. It exhibits excellent mold release characteristics and does not require mold lubrication. Fattibase is a solid with a melting point of 35° C to 37° C, has a specific gravity of 0.890 at 37° C, is opaque white, and is free of suspended matter.

Glycerin-Gelatin Bases: Two types of glycerin and gelatin bases have been developed. First, the glycerin, gelatin and sodium stearate mixtures are designed primarily for prompt evacuation. Second, the glycerin and gelatin water bases, to which medications have been added, have been used for both rectal and vaginal applications. Glycerinated gelatin suppositories, composed of 70% glycerin, 20% gelatin and 10% water, should be packaged in tight containers as they are hygroscopic. Even though they have been occasionally used, they are not recommended as a rectal suppository base as they may exert an osmotic effect and a defecation reflex. Glycerin base is now composed of glycerin (91%), sodium stearate (4%), and purified water (5%). These bases have occasionally been used for the preparation of vaginal suppositories. Glycerin suppositories are still commonly used for their laxative effect.

Water-soluble and Water-miscible Polymer Bases: The main members of this group are bases of polyethylene glycols and poloxomers. Polyethylene glycols are polymers of ethylene oxide and water, prepared to various chain lengths, molecular weights, and physical states. They are available in a number of molecular weight ranges and melting ranges. The numerical designations refer to the average molecular weights of each of the polymers. Polyethylene glycols having average molecular weights of 300, 400, and 600 are clear, colorless liquids. Those having average molecular weights of greater than 1000 are wax-like, white solids with the hardness increasing with an increase in the molecular weight. Various combinations of these polyethylene glycols may be combined by fusion, using two or more of the various types to achieve a suppository base of the desired consistency and characteristics.

In polyethylene glycol based suppositories, the drug is released as a consequence of the progressive dissolution of PEG into the intrarectal aqueous phase. The drug concentration in this small intrarectal phase produces the gradient against the large volume of the plasmatic phase, which regulates the diffusion rate through the barrier. Similar to the use of lipophilic bases, drug solubility in water is an important factor influencing release. PEG influences both in vitro drug availability considerably, by increasing both drug solubility and dissolution rate.

In the intrarectal compartment, the osmotic effect of PEG influences the increase in volume of the aqueous phase.

PEG suppository bases are the most popular water soluble bases. Their advantage lies in the fact that the ratios of the low to the high molecular weight individual PEGs can be altered to prepare a base with a specific melting point or one that will overcome any problems that result from having to add excess powder or liquid to a suppository.

Polybase™ is a preblended suppository base. A white solid, it consists of a homogeneous mixture of PEGs and polysorbate 80. It is a water miscible base that is stable at room temperature, has a specific gravity of 1.177 at 25° C with an average molecular weight of 3440, and does not require mold lubrication.

Poloxomers (Pluronics L44, L62, L64 and F68) have been investigated as potential suppository bases. The Pluronics have practically no odor or taste. Example suppositories can be prepared containing the following formula:

Pluronic F68	1.5 g
Pluronic L44	1.0 mL

Prepare by placing the F68 and L44 in a beaker and melting on a water bath. Remove the beaker from the water bath, stir the mixture thoroughly, and pour into a mold. After hardening, remove from the mold.

Special Suppositories-From the Literature

There has been a lot of research in the past 25 years related to the suppository dosage form. Some of the unique suppositories studied include the following.

Hollow-Type Suppositories: Morphine sulfate suppositories were prepared (1) in an oleaginous base, (2) as a hollow-type suppository containing a controlled release morphine tablet-MS Contin, and (3) as a hollow-type suppository containing morphine powder packed in the hollow space. In vitro release tests and in vivo rectal absorption experiments in rabbits were conducted. From this study, the authors concluded that a satisfactory sustained release morphine suppository for the treatment of cancer pain, administered twice a day using the morphine sulfate powder packed in a hollow-type suppository is effective due to its fast analgesic effect and sustained release nature not only for cancer pain but also for surgical operations.[1]

Another study on enhancing the absorption of gentamicin (GM) from hollow type suppositories used sodium salicylate (SA) or sodium caprylate (CA) as absorption-enhancing agents. Two types of hollow type suppositories were used; a conventional type (Type I) and a release-restricted type (Type II). Without either the SA or CA, there was no GM absorption. However, when SA or CA was added, the bioavailability of GM was 58% with SA and 59% with CA. Further study was done on the Type I suppository using SA or CA in solid or aqueous solution form with the GM. The powdered GM with SA or CA appeared to provide higher plasma levels than when in solution form. The results from this study suggested that the form and concentration of the drug should not be ignored in evaluating the enhancing effects of SA or CA on the rectal absorption of poorly soluble drugs, such as GM.[2]

Hydrogel Suppositories: A study on the morphine hydrogel suppository (MHS) was evaluated in two different configurations. The MHS is a monolithic sustained release rectal preparation. The first configuration (MHS-B) provided a high initial release rate followed by a constant release for the rest of the 12 hour period. The second (MHS-S) provided the same constant release rate for 12 hours. The concentration of morphine was designed to be greatest at the outer and inner surfaces of the suppository which was to provide a release profile closest to that thought to be ideal. The hydrogels have characteristics that contribute to their use for sustained administration of drugs. They are biologically inert. Rehydration and drug release are predictable. The drug concentration can be varied to provide for different release rates. In fact, the dehydrated form can even be cut in half to modify the dose even more. The results of this study indicated that MHS may be of value in the management of postoperative pain.[3]

Layered-Double or Triple Suppositories: Suppositories can be prepared in multiple parts or layers by casting two or three different types of excipients, and can even be colored differently. The advantage is the possibility of isolating one or more incompatible active ingredients from each other. For example, a 3-layer suppository can be prepared by a first layer of the first active drug, followed by a middle layer of a drug-free base, then the third layer of the second active drug. This does require casting in 3 or even 4 different layers; however, it can be done if necessary. Obviously, the different layers must be sufficiently adhered to each other so they will not separate on handling or during administration. In one study, the authors investigated the pharmacokinetics of nifedipine after intravenous injection and rectal administration of conventional suppositories and of sustained-release suppositories in rabbits. Rectal absorption demonstrated about 62-80% bioavailability on average. Using the sustained release suppositories, the mean absorption time was about 6 times greater than that of the conventional suppository. In summary, the dissolution process was the rate-determining step in the sustained release suppository. The conventional suppositories were prepared from PEG 4000 and the sustained release were prepared as a double layer suppository.[4]

Sectile or Bisected Suppositories: Symmetrical suppositories can be composed of two opposite parts separated by means of a beveled edge (bisect) in the middle of the suppository. The purpose here is that a half suppository can be administered to a child and the whole suppository to an adult. The manufacturing process would be the same but the mold would have a different shape to form the bisected suppositories. One must be cautious not to make the bevel too deep that the suppository accidentally breaks during handling or administration.

Reversed-Micellar-Solution (RMS) Suppositories: Diclofenac sodium was prepared as reverse micellar solutions (RMS) and encapsulated in soft gelatin capsules. The reverse micellar solution was prepared by dissolving isopropyl myristate in lecithin at a temperature of 60° C with stirring obtaining a yellowish solution. The diclofenac sodium and propylene glycol were added with continued stirring for about 2 hours. The composition of the RMS was diclofenac sodium 4.75%, lecithin 27.075%, isopropyl myristate 63.175% and propylene glycol 5%, w/w. When coming in contact with aqueous media, the formulation exhibited an application-induced transformation into a semisolid system of liquid crystals which slowed down the rate of drug release. The soft gelatin capsule formulation was shown to be bioequivalent in terms of the AUC with the diclofenac suppositories.[5]

Sustained Release Suppositories-Cellulose Derivatives: A study by Moolenaar and team had the objective of comparing the efficacy, safety and pharmacokinetics of a newly developed controlled-release suppository with MS Contin tablets in cancer patients with pain. The fatty suppositories were prepared using morphine sulfate pentahydrate, Aerosol OT, hydroxypropyl methylcellulose (HPMC), and Witepsol W25. The molten mixture was poured into plastic molds (3 mL) and stored at 4° C. Each suppository contained 30 mg morphine sulfate, 108 mg Aerosol R972, 300 mg HPMC 4000 and 2390 mg Witepsol W25. There were no significant differences in pain intensity scores between the oral and rectal dosage forms within the groups, regardless of the treatment sequence. No treatment differences in nausea, sedation or the demand on escape medication between rectal and oral dosage forms was observed. The authors concluded that the newly developed controlled-release suppository is safe and effective and may be a useful alternative for oral morphine administration in patients with cancer pain.[6]

Sustained Release Suppositories-Carboxyvinyl Polymer: Carboxyvinyl polymer was investigated as an agent to produce sustained release diclofenac sodium suppositories or sodium benzoate suppositories in a triglyceride base containing other water-soluble polymers, such as xanthan gum and polyvinyl alcohol. The suppositories containing carboxyvinyl polymer revealed a twofold longer half-life time as compared to those not containing the polymer.[7]

Sustained Release-Alginic Acid Suppositories: Morphine was incorporated into sustained-release suppositories using alginic acid as the prolonged releasing agent. Witepsol S-55 or W-35 gave higher plasma peak levels than H-15 or E-75. The prolonged release could be altered by the amount of alginic acid added. The suppositories were made by mixing alginic acid with the morphine in the suppository base. The Witepsol bases were preferable to the macrogol bases for the rectal absorption of morphine.[8]

Thermo-Reversible-Liquid Suppository: Propranolol formulated as liquid mucoadhesive suppositories were prepared by adding mucoadhesive polymers (0.6%) to a formulation of thermally gelling suppositories that contained poloxamer 407 (15%), poloxamer 188 (15%) and propranolol HCl (2%). Mucoadhesive polymers used included hydroxypropyl cellulose, polyvinyl-pyrrolidone, carbopol, polycarbophil and sodium alginate.

Rectal bioavailability increased as the mucoadhesive force increased. Retaining propranolol at the dosed site in the rectum by the addition of the mucoadhesive appeared to be very important in voiding first-pass hepatic elimination and increasing the bioavailability of the drug. Among the mucoadhesive polymers examined, sodium alginate and polycarbophil exhibited the largest mucoadhesive force and the smallest intrarectal migration providing the greatest bioavailability of propranolol (84.7 and 82.3% respectively).[9]

Effervescent Suppository: An effervescent base containing citric acid and sodium bicarbonate was made by compressing the powders together. This was further modified by incorporating the powders as an inner pellet of tartaric acid and sodium bicarbonate dispersed in cocoa butter surrounded by a carrageenin-gelatin and medicinal shell. Upon administration, the absorption of water causes effervescence which breaks the suppository apart and forms a froth for dispersing the medication.

COMPOUNDING FORMULAS-SUPPOSITORIES

ABHR Suppository (Ativan-Benadryl-Haldol-Reglan Suppository)

Ativan (lorazepam)	0.5 mg
Benadryl (diphenhydramine)	25 mg
Haldol (haloperidol)	0.5 mg
Reglan (metoclopramide)	10 mg
Fattibase	2.25 g

Melt the Fattibase at about 50° C. Slowly and with stirring, sprinkle the powders on the surface of the melted Fattibase and mix well. Remove from heat and cool until still fluid and pourable. Pour into a suitable mold. Cool and trim, if necessary. Package and label.

Antiemetic Suppository

Metoclopramide hydrochloride	40 mg
Haloperidol	1 mg
Lorazepam	1 mg
Benzotropine	0.5 mg
Fattibase	1.87 g
Optional Ingredients:	
Dexamethasone	20 mg
Diphenhydramine HCl	25 mg

Triturate the powders together until uniformly mixed. If tablets are used as the source of a drug, pulverize those first; if capsules, empty the capsules, then blend in the remaining powders. Melt the Fattibase at about 50° C. Slowly and with stirring, sprinkle the powders on the surface of the melted Fattibase and mix well. Remove from heat and allow to cool until still fluid and pourable. Pour into a suitable mold. Cool and trim, if necessary. Package and label.

Aspirin Suppositories

Pluronic F68	6.00 g
Pluronic L44	7.00 mL
Aspirin	1.02 g

Place the Pluronics in a beaker on a water bath and heat until melted. Add the aspirin and stir the mixture until uniform. Pour the solution in a mold, allow to cool, and remove the suppositories. Package and label.

Belladonna and Opium Suppository, Modified

Belladonna extract	15 mg
Morphine sulfate	7.5 mg
Fattibase	1.75 g

Triturate the powders together until uniform. Melt the Fattibase at about 50° C. Slowly and with stirring, sprinkle the powders on the surface of the melted Fattibase and mix well. Remove from heat and cool until still fluid and pourable. Pour into a suitable mold. Cool and trim, if necessary. Package and label.

Carbamazepine Suppository

	100 mg	200 mg
Carbamazepine	100 mg	200 mg
Bentonite	200 mg	200 mg
Polybase	1.7 g	1.6 g

Heat the Polybase until fluid. Add the bentonite powder and mix until uniform. Slowly and with stirring, sprinkle the carbamazepine powder on the surface of the melt. Remove from heat and cool slightly until still fluid and pourable. Pour into a suitable mold. Cool and trim, if necessary. Package and label.

Chloral Hydrate 500 mg Suppository

Chloral hydrate	500 mg
Polybase	1.75 g

Melt the Polybase to about 55-57° C. Slowly and with stirring, incorporate the chloral hydrate into the melted Polybase and mix well. Remove from heat and allow to cool until still fluid and pourable. Pour into a suitable mold. Cool and trim, if necessary. Package and label.

Chloroquine 300 mg Suppository

Chloroquine phosphate	500 mg
(equivalent to 300 mg chloroquine)	
Polybase	1.7 g

Melt the Polybase to about 55-57° C. Slowly and with stirring, sprinkle the chloroquine phosphate powder on the surface of the melted Polybase and mix well. Remove from heat and allow to cool until still fluid and pourable. Pour into a suitable mold. Cool and trim, if necessary. Package and label.

Diazepam 10 mg Suppository

Diazepam	10 mg
Fattibase	1.9 g

Melt the Fattibase until fluid. Slowly and with stirring, sprinkle the diazepam powder on the surface of the melted Fattibase and mix well. Remove from heat and allow to cool until still fluid and pourable. Pour into a suitable mold. Cool and trim, if necessary. Package and label.

Dihydroergotamine 2 mg Suppository

Dihydroergotamine mesylate	2 mg
Silica gel	20 mg
Fattibase	2.28 g

Melt the Fattibase until fluid. Slowly and with stirring, sprinkle the dihydroergotamine mesylate and silica gel powder on the surface of the melted Fattibase and mix well. Remove from heat and allow to cool until still fluid and pourable. Pour into a suitable mold. Cool and trim, if necessary. Package and label.

Ergotamine Tartrate-PB Suppository

Ergotamine tartrate	2 mg
Caffeine, anhydrous	100 mg
Belladonna powder	20 mg
Pentobarbital sodium	60 mg
Tartaric acid	4 mg
Lactose	40 mg
Fattibase	2.054 g

Melt the Fattibase until fluid. Mix the ergotamine tartrate, caffeine, belladonna, pentobarbital sodium, tartaric acid and lactose powders together. Slowly and with stirring, sprinkle the powder mixture on the surface of the melted Fattibase and mix well. Remove from heat and allow to cool until still fluid and pourable. Pour into a suitable mold. Cool and trim, if necessary. Package and label.

Etodolac 200 mg Suppository

Etodolac	200 mg
Polybase	1.9 g

Melt the Polybase to about 55-57° C. Slowly and with stirring, sprinkle the etodolac powder on the surface of the melted Polybase and mix well. Remove from heat and allow to cool until still fluid and pourable. Pour into a suitable mold. Cool and trim, if necessary. Package and label.

Hydrocortisone 100 mg Mucoadhesive Suppository

Hydrocortisone	100 mg
Karaya gum	500 mg
Polybase	1.4 g

Heat the Polybase to about 55-57° C. Slowly and with stirring, sprinkle the hydrocortisone powder on the surface of the melted Polybase and mix well. Sprinkle the karaya gum mixture on the surface of the mixture and mix until uniform. Remove from heat and allow to cool until still fluid and pourable. Pour into a suitable mold. Cool and trim, if necessary. Package and label.

Migraine Headache Suppository

Ergotamine & Caffeine Tablets	#2
Hyoscyamine sulfate	0.25 mg
Pentobarbital sodium	50 mg
OR	
Metoclopramide	50 mg
OR	
Promethazine	12.5 mg
Fattibase	1.9 g

Pulverize the tablets to a fine powder. Melt the Fattibase until fluid. Slowly and with stirring, sprinkle the powders on the surface of the melt. Remove from heat and cool slightly but it must still remain fluid and pourable. Pour into a suitable mold. Cool and trim, if necessary. Package and label.

Morphine Sulfate 10 to 100 mg Suppository

Morphine sulfate	10 to 100 mg
Fattibase	1.95 to 1.99 g

Melt the Fattibase until fluid. Slowly and with stirring, sprinkle the morphine sulfate on the surface of the melt. Remove from heat and cool slightly but it must still remain fluid and pourable. Pour into a suitable mold. Cool and trim, if necessary. Package and label.

Morphine Sulfate 25 mg or 50 mg Slow Release Suppository

Morphine sulfate	25 or 50 mg
Alginic acid	500 mg
Witepsol H-15	1.75 g

Melt the Witepsol H-15 base until fluid. Slowly and with stirring, sprinkle the morphine sulfate followed by the alginic acid on the surface of the melt. Remove from heat and cool slightly but it must still remain fluid and pourable. Pour into a suitable mold. Cool and trim, if necessary. Package and label.

Nifedipine, Lidocaine and Nitroglycerin Suppository

Nifedipine	7 mg
Lidocaine HCl	30 mg
Nitroglycerin 0.3 mg tablets	#1
Polybase or Fattibase qs	2.5 g

Note: This preparation should be prepared in a room with subdued light due to the light-sensitivity of the nifedipine. Calibrate the suppository mold using the Polybase or the Fattibase. Mix the nifedipine and lidocaine powders together. Levigate the nitroglycerin tablets with a small quanitity of ethyl alcohol. Gently melt the selected base. Add the powders and the nitroglycerin to the melted base and mix well. Pour into molds and allow to cool. Cool, trim, package and label.

Phenytoin 200 mg Suppository

Phenytoin	200 mg
Fattibase	2.28 g

Melt the Fattibase until fluid. If phenytoin capsules are used, they must be the fast-release capsules; it is best if the phenytoin powder is used. Slowly and with stirring, sprinkle the phenytoin powder on the surface of the melted Fattibase and mix well. Remove from heat and allow to cool until still fluid and pourable. Pour into a suitable mold. Cool and trim, if necessary. Package and label.

Promethazine Hydrochloride 25 mg Suppository

Promethazine hydrochloride	25 mg
Fattibase	1.99 g

Melt the Fattibase until fluid. Slowly and with stirring, sprinkle the promethazine hydrochloride powder on the surface of the melt. Remove from heat and cool slightly but it must still remain fluid and pourable. Pour into a suitable mold. Cool and trim, if necessary. Package and label.

Trimethobenzamide 100 mg Suppository

Trimethobenzamide	100 mg
Fattibase	1.95 g

Melt the Fattibase until fluid. Slowly and with stirring, sprinkle the trimethobenzamide powder on the surface of the melt. Remove from heat and cool slightly but it must still remain fluid and pourable. Pour into a suitable mold. Cool and trim, if necessary. Package and label.

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Please circle the most appropriate answer for each of the following questions. There is only ONE correct answer per question.

1. Suppositories are used in therapy to:
   I. promote defecation
   II. introduce drugs into the body
   III. treat anorectal disease
   A. I only
   B. III only
   C. I and II only
   D. II and III only
   E. I, II and III

2. A drug that is absorbed more rapidly in the rectum is:
   A. very soluble in the suppository base.
   B. insoluble in the rectal mucosal fluids.
   C. insoluble in the suppository base and soluble in the rectal mucosal fluids.
   D. soluble in the suppository base and insoluble in the rectal mucosal fluid.
   E. insoluble in both the suppository base and rectal mucosal fluids.

3. To release a drug, a suppository must do which of the following after administration:
   I. dissolve
   II. melt
   III. absorb water and expand
   A. I only
   B. III only
   C. I or II only
   D. II or III only
   E. I, II and III

4. The most frequntly used type of suppository base is the:
   A. fatty Base
   B. water soluble
   C. glycerin-gelatin
   D. natural gum
   E. effervescent

5. Which of the following are fatty type bases?
   I. Fattibase
   II. Wecobee
   III. Witepsol
   A. I only
   B. III only
   C. I and II only
   D. II and III only
   E. I, II and III

6. Which of the following have been used as absorption enhancers?
   I. sodium caprylate
   II. sodium salicylate
   III. cocoa butter
   A. I only
   B. III only
   C. I and II only
   D. II and III only
   E. I, II and III

7. Which type of special suppository can be used to seperate incompatible ingrediants?
   A. hollow
   B. layered
   C. bisected
   D. reversed-micellar-solution
   E. effervescent

8. Which of the following special suppositories will form a froth upon administration?
   A. effervescent
   B. hollow
   C. layered
   D. bisected
   E. sustained release-cellulose derivative

9. A suppository prepared from Pluronic F68 and Pluronic L44 belongs to which class of suppository bases?
   A. effervescent
   B. reversed-micellar-solution
   C. oleaginous
   D. water soluble-water miscible
   E. collagen

10. In which of the following bases must the drug "partition" from the oil phase to the aqueous mucosal fluids?
    A. fatty acid
    B. poloxamer
    C. effervescent
    D. glycerin-gelatin
    E. polyethylene glycol

11. My practice setting is:
    A. Community-based
    B. Managed care-based
    C. Hospital-based
    D. Consultant and other

12. The quality of the information presented in this article was:
    A. Excellent B. Good C. Fair D. Poor

13. The test questions correspond well with the information presented.
    A. Yes B. No

14. Approximately how long did it take you to read the Secundum Artem article AND respond to the test questions?

    _____

15. What topics would you like to see in future issues of Secundum Artem?

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