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Secundum Artem

Current & Practical Compounding Information for the Pharmacist.

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Compounding Rectal Dosage Forms, Part I

GOALS AND OBJECTIVES

Goal: To provide information and support for dosage forms that can be compounded and administered rectally.

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

1. List at least five advantages to the rectal administration of drugs.
2. Describe the anatomy and physiology of the rectum.
3. Discuss the factors involved in drug release from different matrices administered rectally.
4. Discuss the characteristics of enemas, microenemas, gels, ointments and aerosols administered rectally.
5. Describe the formulation variables that must be considered in compounding rectal dosage forms.

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

Introduction

Rectal administration is not often the first route of choice; but it becomes a good alternative when the oral route is inadvisable. Relatively low cost and lack of technical difficulties make rectal drug administration attractive when compared to parenteral therapy. The downside of rectal administration includes the esthetics and stigma of violating the patient's dignity. This, along with potential rectal irritation due to frequent administration, and difficulty in titrating a correct dose due to limited strengths of commercial rectal dosage forms pose some challenges.

Psychologically, rectal dosage forms can provide a considerable placebo effect in the treatment of anorectal disorders. The user feels that something is really being done at the involved site and this can produce a positive attitude towards this mode of treatment of the disease or disorder. This may promote hope and the possibility of avoiding the embarrassment of telling the family and friends of what is happening in the private area.

Previously, the rectal pathway was reserved for the administration of locally active products such as those in the treatment of hemorrhoids, worms and constipation. In the treatment of hemorrhoids and anal fissures, a suggestion was made at one time that a suppository should be "hour glass" or "collar button" shaped so that the suppository would stay in the anal canal.

Now, it is well accepted that many active ingredients can be administered rectally and achieve therapeutic blood levels from any of several different dosage forms. Some medications are best administered by this route while others can be if needed.

Advantages to Rectal Administration:

The advantages to rectal administration include the following.

1. First pass effect - Avoiding, at least partially, the first pass effect which may result in higher blood levels for those drugs subject to extensive first pass metabolism upon oral administration.
2. Drug stability - Avoiding the breakdown of certain drugs that are susceptible to gastric degradation.
3. Large dose drugs - Ability to administer somewhat larger doses of drugs than using oral administration.
4. Irritating drugs - Ability to administer drugs which may have an irritating effect on the oral or GI mucosa when administered orally.
5. Unpleasant tasting or smelling drugs - Ability to administer unpleasant tasting or smelling drugs whose oral administration is limited.
6. In children, the rectal route is especially useful. An ill child may refuse oral medication and may fear injections.
7. Rectal administration can be especially useful in terminal care.

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Rectal administration provides for a rapid, and in many cases, extensive absorption of the active ingredient. The rapidity, intensity and duration of action are three parameters which must be considered during formulation for rectal administration and, in many cases, can be altered to meet the needs of the individual patient.

Anatomical and Physiological Considerations

The rectum consists of the last few inches of the large intestine, terminating at the anus. The wall of the GI tract consists of several layers, including the mucosa, submucosa, tunica muscularis and the visceral peritoneum. The mucous membrane of the rectum, where rectal dosage forms are generally administered, is made up of a layer of cylindrical epithelial cells, differentiated from those of the intestine by the absence of villi.

The rectum contains three types of hemorrhoidal veins, namely the superior hemorrhoidal vein, middle hemorrhoidal vein, and the inferior hemorrhoidal vein. These veins act by transporting the active principle absorbed in the rectum to the blood system either directly by means of iliac veins and the vena cava (inferior and middle hemorrhoidal veins) or indirectly by means of the portal vein and the liver (superior hemorrhoidal vein).

The three hemorrhoidal veins are linked by an anastomosis network. Since it is not really possible to predict the position or exact location of the dosage form in the rectum, it is not really possible to predict exactly which way the active principle will be transported. It may preferably be by one pathway or another or a combination. However, it is generally accepted that at least 50% to 70% of the active ingredients administered rectally take the direct pathway, thus bypassing the liver and avoiding the first-pass effect. There is also the possibility of absorption into the lymphatic vessels that should not be dismissed, but may be minimal.

Physiology

The physiological factors likely to affect rectal absorption are the rectal liquid pH and the rectal liquid buffering capacity. The rectal mucosal fluid has a pH very close to neutral and has a low buffer capacity. Hence, after administration of the suppository, the pH of the rectal liquid may be determined by the active principle being used. These facts lead us to conclude that the addition of buffering agents of a suitable pH range to the suppositories could, in some cases, increase active principle absorption.

When empty of fecal material, the rectum contains only 2 to 3 mL of inert mucosal fluid. In the resting state, the rectum is nonmotile and there are no villi or microvilli present on the rectal mucosa. However, there is abundant vascularization of the submucosal region of the rectum wall with blood and lymphatic vessels.

Among the physiologic factors that affect drug absorption from the rectum are the colonic contents, circulation route, and the pH and lack of buffering capacity of the rectal fluids.

Colonic Content: When systemic effects are desired from the administration of a medication, greater absorption may be expected from a rectum that is void than from one that is distended with fecal matter. A drug will obviously have greater opportunity to make contact with the absorbing surface of the rectum and colon in the absence of fecal matter. Therefore, when deemed desirable, an evacuant enema may be administered and allowed to act before administration of a suppository of a drug to be absorbed. Other conditions such as diarrhea, colonic obstruction due to tumorous growths, and tissue dehydration can all influence the rate and degree of drug absorption from the rectal site.

Circulation route: It is estimated that about 50-70% of the dose of a rectal dosage form that is absorbed will bypass the liver into the general circulation.

pH and Lack of Buffering Capacity of the Rectal Fluids: Because rectal fluids are essentially neutral in pH (7–8) and have negligible buffer capacity, the form in which the drug is administered will not generally be chemically changed by the rectal environment; therefore the pH of the medium may be determined by the characteristics of the drug and the dosage form.

Formulation Variables

Active drugs have a number of physical characteristics that can affect efficacy. For rectal dosage forms, those of interest involve the following:

1. The nature and form of the active principle (esters, salts, complexes, etc).
2. The physical state, particle dimensions and the specific surface of the product.
3. The presence or absence of adjuvants added to the active principle.
4. The nature and type of dosage form in which the active principle is incorporated.
5. Pharmaceutical procedures used in the preparation of the dosage form.

Physical State: An active drug can be either a solid, liquid or semisolid in nature. For solids, the drug's particle size may be very important, especially if the drug is not very water soluble; the increase in surface area resulting from decreased particle size can serve to enhance its activity.

Solubility: Whether or not the active ingredient is soluble in the vehicle can alter the manufacturing and compounding processes in several ways. Increased solubility of the active in the base can improve product homogeneity; however, it may also delay the release of the active if there is too great an affinity of the drug for the vehicle. In some cases, it may be desired to retain the drug in the rectal cavity for a longer time and this can be accomplished if the drug has a greater affinity for the vehicle than for migrating to the mucosal surface for absorption or to produce a local effect.

If the active ingredient is insoluble in the vehicle, as is the case when a "suspension" or "emulsion" is formed, this poses different problems. It is necessary to maintain homogeneity of the total mixture; this can usually be obtained by constant agitation of the mixture during processing and filling. Emulsions can be handled through the proper use of surfactants to obtain a homogenous mixture.

Related to the water solubility of a drug can be the rate of diffusion across the rectal membrane. A drug with high water solubility quickly leaves the vehicle, producing a high concentration in the intrarectal phase which supports a high diffusion rate across the barrier. A drug with low water solubility saturates the intrarectal phase at a low concentration resulting in low diffusion and subsequent low dissolution of the drug particles remaining in the melted excipient. Drugs with low solubility in water may result in low availability, while drugs with good solubility may give a rapid and intense therapeutic response with the dose administered.[1]

A number of factors affect the decisions the pharmacist must make when preparing a rectal dosage form. Questions the pharmacist should ask before formulating this dosage form include the following:

- Is the desired effect to result from systemic or local use?
- Is the dosage form a liquid, semisolid or solid?
- Is a rapid or a slow and prolonged release of the medication desired?

Drugs for local effect may include the treatment of hemorrhoids, local anesthetics, antiseptics, antibiotics, and antifungals. Drugs for systemic effect include analgesics, antiasthmatics, antinauseants, antiepileptics, hormones and others.

The selection of a vehicle is dependent upon a number of physicochemical variables, including the characteristics of the drug, the base and other excipients that are present.

Drug Release: The rate of drug release is an important factor in the selection of a vehicle. If a drug does not release its medication within 6 hours, the patient may not receive its full benefit, as the drug remaining in the rectum may be expelled. Thus, among the factors that must be considered in the selection of a suppository base is the drug's solubility. One way to ensure maximum release of the drug from the base is to apply the principle of opposite characteristics, i.e., water soluble drugs should be placed in oil soluble bases while oil soluble drugs should be placed in water soluble bases.

Drug release rate requirements are especially important in the selection of the suppository base. Other factors must also be considered when preparing a suppository. They include the presence of water, hygroscopicity, viscosity, brittleness, density, volume contraction, special problems, incompatibilities, pharmacokinetics, and bioequivalence.

Presence of Water: When preparing nonaqueous rectal dosage forms, the pharmacist should avoid using water to incorporate an active drug as water may accelerate the oxidation of fat, increase the degradation rate of many drugs, enhance reactions between the drug and other components, support bacterial/fungal growth, and require the addition of bacteriostatic agents. Furthermore, if the water evaporates, the dissolved substances may crystallize and possibly become irritating upon insertion.

Hygroscopicity: Glycerin and polyethylene glycol containing vehicles are hygroscopic. The rate of moisture change is dependent on the chain length of the molecule as well as the temperature and humidity of the environment.

Viscosity: Viscosity considerations are also important in the preparation and the release of the drug. If the viscosity of a base is low, it may be necessary to add a thickening agent to ensure uniformity of the drug in the vehicle. After the dosage form has been administered, the release rate of the drug may be slowed if the viscosity of the vehicle is very high. This is because the viscosity causes the drug to diffuse more slowly through the base to reach the mucosal membrane for absorption.

Brittleness: Brittle suppositories can be difficult to handle, wrap, and use. In general, brittleness results when the percentage of nonbase materials exceeds about 30%. Synthetic fat bases with high stearate concentrations or those that are highly hydrogenated are typically more brittle. Shock cooling also causes fat and cocoa butter suppositories to crack. This condition can be prevented by ensuring that the temperature of the mold is as close to the temperature of the melted base as possible. Suppositories should not be placed in a freezer, which also causes shock cooling. The addition of a small quantity (usually less than 2%) of Tween 80, Tween 85, fatty acid monoglycerides, castor oil, glycerin, or propylene glycol will make these bases more pliable and less brittle.

ENEMAS/MICROENEMAS (SOLUTIONS/SUSPENSIONS)

Enemas

Enemas are dosage forms designed to be administered rectally for clearing out the bowel or for administration of drugs or food. An enema is a method of administration and may involve solutions, suspensions, emulsions, foams, and gels. Generally, there are two types: retention enemas and evacuation enemas.

Retention Enemas: A number of solutions, suspensions and emulsions are administered rectally for the local effects of the medication (e.g., hydrocortisone) or for systemic absorption (e.g., aminophylline). In the case of aminophylline, the rectal route of administration minimizes the undesirable gastrointestinal reactions associated with oral therapy. Clinically effective blood levels of the agents are usually obtained within 30 minutes following rectal instillation. Corticosteroids can be administered as retention enemas as adjunctive treatment of some patients with ulcerative colitis.

Evacuation Enemas: Rectal enemas are used to cleanse the bowel. Commercially, many enemas are available in disposable plastic squeeze bottles containing a premeasured amount of enema solution. The agents present are solutions of sodium phosphate and sodium biphosphate, glycerin and docusate potassium, and light mineral oil.

Enemas may be prepared as solutions, suspensions, emulsions etc.

Solutions: Considerations in preparing solutions include solubility, solvent selection, pH, osmolality and stability of the drug. If the pH is too low or too high, it may be irritating to the mucosa. If the solution is hyperosmolar, it may pull fluids from the local area and initiate a defecation reflex.

Suspensions: Suspensions are preparations containing finely divided drug particles distributed somewhat uniformly throughout a vehicle in which the drug exhibits a minimum degree of solubility. In most good pharmaceutical suspensions, the particle diameter is between 1 and 50 microns. The pharmacist may have to use a solid dosage form, e.g., tablet, capsule, of the drug and extemporaneously compound a liquid preparation, or it can be made from the bulk powder.

Typically, when formulating an extemporaneous suspension, the contents of a capsule, crushed tablets, or bulk powder is placed in a mortar. The selected vehicle is then slowly added to and mixed with the powder to create a paste and then diluted to the desired volume.

To minimize stability problems of the extemporaneously prepared product, it should be placed in air-tight, light-resistant containers by the pharmacist and subsequently stored in the refrigerator by the patient. Because it is a suspension, the patient should be instructed to shake it well prior to use and on a daily basis watch for any color change or consistency change that might indicate a stability problem with the formulation.

The following examples of rectal suspensions have frequently been compounded by pharmacists when not commercially available. Barium Sulfate for Suspension, USP has been employed orally or rectally for the diagnostic visualization of the gastrointestinal tract. Mesalamine (i.e., 5-aminosalicylic acid) suspension was introduced onto the market in 1988 as Rowasa® (Solvay) for treatment of Crohn's disease, distal ulcerative colitis, proctosigmoiditis, and proctitis.

Emulsions: An emulsion is a dispersion in which the dispersed phase is composed of small globules of a liquid distributed throughout a vehicle in which it is immiscible. Pharmaceutically, the process of emulsification enables the pharmacist to prepare relatively stable and homogeneous mixtures of two immiscible liquids. It permits the administration of a liquid drug in the form of minute globules rather than in bulk.

The initial step in preparation of an emulsion is the selection of the emulsifier. Among the emulsifiers and stabilizers for pharmaceutical systems are some carbohydrate materials (acacia, tragacanth, agar, chondrus, and pectin), protein substances (gelatin, egg yolk, and casein), high molecular weight alcohols (stearyl alcohol, cetyl alcohol, and glyceryl monostearate), wetting agents (which may be anionic, cationic, or nonionic), and finely divided solids (colloidal clays including bentonite, magnesium hydroxide, and aluminum hydroxide).

Emulsions may be prepared by several methods, depending upon the nature of the emulsion components and the equipment available for use. On a small scale, as in the laboratory or pharmacy, emulsions may be prepared using a dry Wedgewood or porcelain mortar and pestle, a mechanical blender or mixer such as a Waring blender or a milk-shake mixer, a hand homogenizer, a bench-type homogenizer, or sometimes a simple prescription bottle. On a large scale, large volume mixing tanks may be used to form the emulsion through the action of a high-speed impeller. As desired, the product may be rendered finer by passage through a colloid mill, in which the particles are sheared between the small gap separating a high speed rotor and the stator, or by passage through a large homogenizer, in which the liquid is forced under great pressure through a small valve opening.

Microenemas

A microenema, also called rectal tube, is a more concentrated form of a drug generally administered for a systemic effect. As an example, diazepam microenemas (Stesolid® in Europe) are available, generally containing about 5 mg/mL diazepam in solution. Diazepam microenemas are generally used in the management of selected, refractory patients with epilepsy, on stable regimens of antiepileptic drugs, who require intermittent use of diazepam to control occasional breakthrough seizures.

Microenemas can be easily prepared by adding thickening agents to injectable solutions. This provides the dose of a drug in a reasonably small volume of generally 1 to 5 mL. Microenemas can be administered by attaching a short length of tubing to a syringe in which the microenema has been placed. The tubing is lubricated and inserted rectally, followed by depressing the plunger to deliver the drug. As an alternative, the microenema can be placed in a plastic bulb-device where the tip is lubricated and then inserted rectally and the bulb squeezed to expel the drug.

Gels

Gels are semisolid systems consisting of dispersions made up of either small inorganic particles or large organic molecules enclosing and interpenetrated by a liquid. Some gel systems are as clear as water in appearance and others are turbid, since the ingredients involved may not be completely molecularly dispersed (soluble or insoluble) or they may form aggregates, which disperse light. The concentration of the gelling agents is mostly less than 10%, usually in 0.5 to 2.0% range, with some exceptions.

Gels may be prepared by the direct hydration in water of the inorganic chemical, the hydrated form constituting the disperse phase of the dispersion. Examples of gelling agents include acacia, alginic acid, bentonite, carbomer, carboxymethylcellulose sodium, cetostearyl alcohol, colloidal silicon dioxide, ethylcellulose, gelatin, guar gum, hydroxyethylcellulose, hydroxypropyl cellulose, hydroxypropyl methylcellulose, magnesium aluminum silicate, maltodextrin, methylcellulose, polyvinyl alcohol, povidone, propylene carbonate, propylene glycol alginate, sodium alginate, sodium starch glycolate, starch, tragacanth and xanthan gum.

In gel preparation, the powdered polymers, when added to water, may form temporary gels that slow the process of dissolution. As water diffuses into these loose clumps of powder, their exteriors frequently turn into clumps of solvated particles encasing dry powder. The globs or clumps of gel dissolve very slowly because of their high viscosity and low diffusion coefficient of the macromolecules.

Rectal lubricating jellies are used to assist in medical procedures, to aid in insertion of various devices and drugs, including catheters and suppositories, and as vehicles for some drug products, especially in extemporaneous compounding.

Rectal Ointments

The use of rectal ointments is generally limited to the treatment of local conditions. Ointments can be for topical application to the perianal area and for insertion within the anal canal. They mostly are used to treat local conditions of anorectal pruritus, inflammation and the pain and discomfort associated with hemorrhoids. The drugs employed include astringents (e.g., zinc oxide), protectants and lubricants (e.g., cocoa butter, lanolin), local anesthetics (e.g., pramoxine HCl), and antipruritics and anti-inflammatory agents (e.g., hydrocortisone).

The bases used in anorectal ointments and creams include combinations of polyethylene glycol 300 and 3350, emulsion cream bases utilizing cetyl alcohol and cetyl esters wax, and white petrolatum and mineral oil. When antimicrobial preservatives are required, methylparaben, propylparaben, benzyl alcohol, and butylated hydroxyanisole (BHA) are frequently used.

Before applying rectal ointments and creams to the perianal skin, the affected area should be cleansed and dried by gentle patting with toilet tissue. Then a portion of the ointment or cream is placed on a tissue and a thin film is gently spread over the affected area. Products having a water-washable base are easier to spread and remove after application and tend to stain clothing less than products having an oleaginous base.

Rectal ointments and creams may be dispensed with special perforated plastic tips for products to be administered into the anus, primarily in the treatment of the pain and inflammation associated with hemorrhoids. Before use, the rectal tip should be thoroughly cleaned, screwed onto the ointment tube in place of the cap, and lubricated with mineral oil or a lubricating jelly. Anusol® and Tronolane® are examples of rectal ointments used in the treatment of hemorrhoids.

Aerosols

Although occassionally used rectally, these are not generally suitable for compounding. Pharmaceutical aerosols are pressurized dosage forms containing one or more active ingredients which upon actuation emit a fine dispersion of liquid and/or solid materials in a gaseous medium. Pharmaceutical aerosols are similar to other dosage forms because they require the same types of considerations with respect to formulation, product stability, and therapeutic efficacy. However, they differ from most other dosage forms in their dependence upon the function of the container, its valve assembly, and an added component—the propellant—for the physical delivery of the medication in proper form.

Aerosol products may be designed to expel their contents as a fine mist, a coarse, wet or a dry spray, a steady stream, or as a stable or a fast-breaking rectal foam. The physical form selected for a given aerosol is based on the intended use of that product.

Rectal Aerosols

Rectal aerosol foams are commercially available containing anti-inflammatory agents. The aerosol package contains an inserter device used to direct the foam when activated. The foams are generally oil-in-water emulsions, resembling light creams. Some available commercial preparations of rectal foams use rectal inserters for the presentation of the foam to the anal canal. Products such as ProctoFoam® (pramoxine hydrochloride) and Proctofoam®-HC (with hydrocortisone) are used to relieve inflammatory anorectal disorders. These products are accompanied by applicators to facilitate administration. When ready to use, the applicator is attached to the aerosol container and filled with a measured dose of product. The applicator is then inserted into the anus and the product delivered by pushing the plunger of the applicator. After removal, the applicator and the patient's hands should be thoroughly washed.

Compounding Formulas
Enemas/Microenemas-Solutions/Suspensions/Emulsions

Diazepam 5 mg/mL Rectal Microenema

Diazepam		500 mg
Ethanol 95%		10 mL
Benzoic acid		0.1 gm
Sodium benzoate		4.9 gm
Benzyl alcohol		1.5 mL
Propylene glycol		40 mL
Hydroxypropyl methylcellulose		4.2 gm
Purified water	qs	100 mL

Mix the ethanol, propylene glycol and benzyl alcohol together. Add the diazepam and mix until dissolved. Add the hydroxypropyl methylcellulose and mix until dispersed well. Mix the sodium benzoate and benzoic acid in about 40 mL of purified water. Slowly, add this mixture to the propylene glycol mixture and mix well. Add sufficient purified water to volume, mix well, and allow to stand until the solution is thickened. Package and label.

Hydrocortisone 100 mg Enema

Hydrocortisone, micronized		100 mg
Methylcellulose 2% solution		25 mL
Preserved water	qs	50 mL

Incorporate the micronized hydrocortisone into the methylcellulose solution and mix well. Add sufficient preserved water to volume and mix well. Package and label.

Progesterone 200 mg per 100 mL Enema

Progesterone, micronized		200 mg
Povidone		10 g
Purified water	qs	100 mL

Wet the povidone with about 15 mL of water to form a paste. Use a magnetic stirrer and add about 60 mL of water, stirring until a clear solution is obtained. Add the micronized progesterone and mix well. Add the remaining water to volume and thoroughly mix. Package and label.

Short Chain Fatty Acid Enema

Sodium acetate, trihydrate		817 mg
Sodium propionate		288 mg
Sodium butyrate		440 mg
Sodium chloride		82 mg
Purified water	qs	100 mL

Dissolve the short-chain fatty acids and sodium chloride in about 90 mL of the purified water. Check and adjust the pH if necessary using either 10% sodium hydroxide solution or 10% hydrochloric acid to a pH between 7 and 8. Add sufficient purified water to volume and mix well. Package and label.

Sodium Phosphate Enema Solution

Sodium phosphate, dibasic, anhydrous		19 g
Sodium phosphate, monobasic, anhydrous		7 g
Purified water	qs	118 mL

Dissolve the monobasic and dibasic sodium phosphate in sufficient purified water to volume. Package and label.

Sulfasalazine Enema

Sulfasalazine		3 g
Glycerin		5 mL
Methylcellulose 2% solution	qs	50 mL

Mix the sulfasalazine with the glycerin to form a smooth paste. Geometrically, incorporate the methylcellulose 2% solution to volume and mix well. Package and label.

Gels

Diltiazem Hydrochloride 2% Gel

Diltiazem hydrochloride		2 g
Propylene glycol		10 mL
Hydroxyethylcellulose		2 g
Preserved water	qs	100 mL

Combine the diltiazem hydrochloride with the propylene glycol and mix to form a smooth paste. Incorporate the hydroxyethylcellulose and mix well. Heat the preserved water to about 70° C and slowly incorporate into the propylene glycol mixture and mix well. Package and label.

Nifedipine Gel 160 mg/mL in PLO

Nifedipine		16 g
Diethylene glycol monoethyl ether		10 mL
Lecithin:isopropyl palmitate solution		20 mL
Pluronic F-127 20% gel	qs	100 mL

Combine the nifedipine with the diethylene glycol monoethyl ether to form a smooth paste. Add the lecithin:isopropyl palmitate solution and mix well. Add sufficient Pluronic F-127 20% gel to volume and mix thoroughly, using a mechanical shearing force. Package and label.

Rectal Lubricating Jelly Formula

Methylcellulose, 4000 cps		0.8 gm
Carbopol 934		0.24 gm
Propylene glycol		16.7 mL
Methylparaben		0.015 gm
Sodium hydroxide, qs ad	pH 7	
Purified water, qs ad		100 gm

Disperse the methylcellulose in 40 mL of hot (80–90° C) water. Chill overnight in a refrigerator to effect solution. Disperse the Carbopol 934 in 20 mL water. Adjust the pH of the dispersion to 7.0 by adding sufficient 1% sodium hydroxide solution (about 12 mL is required) and bring the volume to 40 mL with purified water. Dissolve the methylparaben in the propylene glycol. Mix the methylcellulose, Carbopol 934 and propylene glycol fractions using caution to avoid incorporating air. Package and label.

Ointments

Nitroglycerin 0.2% Ointment

Nitroglycerin 2% ointment	10 g
Lanolin, anhydrous	30 g
White petrolatum	60 g

Mix the anhydous lanolin with the white petrolatum. Geometrically, incorporate the lanolin-white petrolaum mixture into the nitroglycerin 2% ointment and mix until uniform. Package and label.

References

1. Readldon N, Ragazzi E, Ragazzi E. Effect of drug solubility on the in vitro availability rate from suppositories with lipophilic excipients. Pharmazie. 2000 May;55(5):372-7.

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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. When administered rectally, at least what percent of the active ingredients will avoid the first-pass effect?
   A. Less than 10%
   B. 10-25%
   C. 25-50%
   D. 50-70%
   E. More than 70%

2. Which of the following factors can affect the efficacy of a rectally administered dosage form?
   I. whether the drug is an ester, salt, or complex
   II. the presence of adjuvants in the formula
   III. the particle size of the drug
   A. I only
   B. III only
   C. I and II only
   D. II and III only
   E. I, II and III.

3. Generally, it is best to keep water out of a fatty acid base suppository rectal dosage form because:
   I. it may accelerate oxidation of fat
   II. it may increase the degradation rate of drugs
   III. it may support bacterial/fungal growth
   A. I only
   B. III only
   C. I and II only
   D. II and III only
   E. I, II and III.

4. Microenemas can be easily prepared by adding what ingredient to an injection?
   A. buffering agent
   B. chelating agent
   C. preservative
   D. surfactant
   E. thickening agent

5. Alginic acid, carbomer, cetostearyl alcohol, hydroxypropyl cellulose, magnesium alminum silicate and povidone are all agents that can be used as:
   A. buffering agents
   B. chelating agents
   C. preservatives
   D. surfactants
   E. gelling agents

6. Which of the following dosage forms can be used to produce a systemic effect of an active drug?
   A. rectal enema
   B. rectal gel
   C. rectal ointment
   D. rectal microenema
   E. all the above

7. Which of the following characteristics may help in increasing the rate of drug absorption?
   I. insoluble in the vehicle
   II. soluble in rectal fluids
   III. very viscous vehicle
   A. I only
   B. III only
   C. I and II only
   D. II and III only
   E. I, II and III.

8. How can viscosity affect a rectal dosage form?
   I. If too high, drug release may be slow
   II. Is needed to help ensure uniformity of suspensions during preparation
   III. Helps minimize degradation of the drug
   A. I only
   B. III only
   C. I and II only
   D. II and III only
   E. I, II and III.

9. Which of the following ingredients are commonly used intrarectally and around the rectal opening?
   A. bismuth subnitrate
   B. diazepam
   C. hydrocortisone
   D. progesterone
   E. methotrexate

10. Microenemas generally consist of the drug in a volume of about:
   A. 1-5 mL
   B. 5-10 mL
   C. 10-15 mL
   D. 15-25 mL
   E. 25-50 mL

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