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CHELATED SUPPOSITORY AND METHOD
OF USING SAMERaymond R. Sackler, Roslyn, N.Y., assignor to Mortimer
D. Sackler and Raymond R. Sackler, Yonkers, N.Y.,
a copartnershipNo Drawing. Continuation-in-part of application Ser. No.
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16 Claims

ABSTRACT OF THE DISCLOSURE

A hydrogen bonded compound as a suppository vehicle comprising a compound of the group gum guar, pectin, algin, carboxymethylcellulose or mixtures of these and a polyoxyethyleneglycol having a molecular weight of from 200 to 6000 or mixtures of these, as a carrier for pharmacologically active substances to be administered by the rectal route when shaped into suppositories, or for rectal administration to provide an anorectal lubricant mucosal film or a laxative action.

This invention relates to new and novel pharmaceutical compositions which are suitable for use as a suppository base and which may be formed into suppositories for rectal insertion, as well as used as a carrier for pharmacologically active substances to be administered by suppository route. In particular, this invention relates to hydrogen-bonded compounds comprising polymeric polyoxyethylene glycol, having a molecular weight of from 200 to 6000, which are hydrogen-bonded to polymeric vegetable polycyclohexose compounds, as for example, gum guar, algin, pectin and carboxymethylcellulose. This hydrogen-bonded compound provides an advantageous carrier for pharmacologically active substances, or it may be formed into suppositories which may be used directly for insertion into the rectum.

This application is a continuation-in-part of my co-pending United States patent application, Ser. No. 376,260, filed June 18, 1964, now U.S. Patent No. 3,325,472, now abandoned which was a continuation-in-part of my then co-pending United States patent application, Ser. No. 296,477, which was filed July 22, 1963 now abandoned.

Suppositories are conical or elliptical medicated solids intended for insertion into one of the several orifices of the body, excluding the mouth. Insertion into the body should be simple and easy, without incidental tissue trauma or pain. After insertion, the suppository should disintegrate readily, that is, either melt, dissolve or disperse, thereby distributing the active therapeutic substances and/or the suppository base within the body cavity. Suppositories should be of a shape to permit the easy insertion into the particular body cavity for which they are intended and be of sufficient weight to provide an indicated therapeutic dose of the drug, when serving as a pharmaceutical carrier.

A suppository may be utilized to obtain either a local or systemic effect. The action of a drug administered by suppository, but which is not absorbed through the mucous membrane lining the orifice of insertion, is considered to be a local effect in contrast to the effect resulting after the use of a suppository from which the active ingredients are absorbed into the systemic circulation. Emollients, astringents, antibiotics and certain anti-inflammatory agents are examples of classes of compound which may be utilized in combination with a suppository base to achieve a local effect, whereas a wide variety of drugs, such as hormones, analgesics, sedatives, alkaloids, certain soluble inorganic and organic synthetic therapeutic compounds, have been

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successfully administered by the suppository route for their systemic effect.

When a drug is absorbed across the mucous membrane surface, the suppository route of administration will usually result in a systemic effect, just as if the drug had been given orally. The principal differences which distinguish the suppository route of administration in these instances, from the oral route of administration, are the onset, duration and intensity of action, all of which are dependent upon the dosage and rate of release and absorption of the active drug from the suppository carrier. The rich blood supply of the tissues of the rectum and vagina provide a suitable means for obtaining a systemic blood level of a drug, thereby avoiding the upper gastrointestinal tract which is not desirable in those instances where individual patient intolerance to a drug, or destruction of the drug by the digestive juices, prevents its oral administration.

Thus, it has been shown that the systemic onset of action of drugs administered by the suppository route may be more prompt than when the same drug is administered orally. The difference in time is usually ascribed to the longer period that such drugs remain in the stomach after oral administration. Thus, for example, in the case of most alkaloids, the pharmacologic response is observed within 3 to 5 minutes after introduction into the rectum by suppository medication, an effect which is much more rapid than that observed after the oral use of the same substance.

Suppositories may be prepared from either water-immiscible fatty substances or water-miscible hydrophilic substances. Among the fatty substances which have been suggested as bases for suppositories are lard, theobroma oil, resins and fats. Among this group of suppository compounds are included such substances as white wax, spermacetic, oleic acid and stearic acid mixtures, and hydrogenated vegetable oils. The aqueous immiscibility of the fatty suppository substance is a general limitation of this class of compounds being used as carriers for certain pharmacologically active polar compounds. The hydrophobic character of the lipid material causes pooling in the essentially aqueous character of the rectum, and thereby inhibits the release and transfer of the active material. This non-uniform distribution of medicament results in both poor absorption and an uneven rate of absorption. Some fatty components, such as white wax and spermaceti, do not melt at body temperature and require other additives to provide a composition which will permit disintegration of the suppository mass at body temperature. The vegetable oils and waxes have still another disadvantage in that rancidity will occur unless suitable preservatives are added, while the use of oleic and stearic acid mixtures is limited for those medicaments which do not react with these acid components. Furthermore, the mixture of organic acids may cause a local tissue irritant effect in some individuals.

In order to avoid the basic limitations of the fatty suppository bases, attention was directed toward hydrophilic aqueous miscible substances, such as the polyoxyethylene glycols, glycerinated gelatin and polymerized ethylene oxide derivatives of glycols. However, as a group, these compounds possess disadvantages which detract from their use and are unsuitable for use with a number of drugs because of pharmaceutical incompatibility. This is especially important when considering drugs which undergo hydrolytic decomposition in the presence of water and the glycols. The aqueous miscible suppository bases are prepared to contain a certain amount of water and also since these bases are hygroscopic, special packaging techniques must be used to maintain their stability under storage conditions. Problems of uniform dispersibility and

disintegration have been encountered with these suppository bases. Since, in general, suppositories prepared with these materials will not melt at body temperature, varying amounts of water are required for their dispersion and because of the limited fluid sometimes available in the rectum, variable results occur.

Suppositories are manufactured by two basic processes—the hot pour technique and the compression-extrusion technique. The hot pour technique involves the pouring of the molten suppository composition into a suitable mold, which is then cooled below the melting point of the suppository base. Upon hardening, it assumes the desired form and shape. The compression-extrusion technique involves the packing of the mold with the suppository base under pressure. This method has the advantage that the base is solid at all times and therefore the dispersed materials do not sediment as they would when liquid compositions are utilized during the hot pour technique. The high speed production of suppositories required by commerce makes the extrusion technique a preferred method. However, this procedure has an inherent limitation in that the elevated pressures required by the high speed production causes an elevated temperature of the suppository base with consequent partial liquefaction. While suitable additives have been devised to maintain both a uniform consistency of the suppository mass as well as a lubricant effect so that the finished suppositories may be readily ejected from the mold, these additives result in a harder suppository which may cause tissue trauma when inserted. The hard suppository is more apt to cause tissue trauma to the sensitive ano-rectal tissues of the infant as well as in those patients presenting ano-rectal disease, such as hemorrhoids, ano-rectal fistula and fissure, or during the immediate post-operative period following proctologic surgery.

Through the use of the products of the present invention, the inherent limitations for both the fatty and the water-miscible bases are avoided. When a polycyclohexose compound, as for example, guar gum, algin, carboxymethylcellulose, and pectin, are mixed with polyoxyethylene glycol having a molecular weight of from 200 to 6000, which are known in commerce as "Carbowaxes," a hydrogen-bonded chelation compound is formed. The new suppository compound is a homogeneous substance, having no reproducible physical and chemical properties and which is capable of being shaped and formed into suppositories which have new desirable and advantageous properties. The new suppository compound is compatible with pharmacologically active substances and disintegrates, both rapidly and uniformly, after insertion into the body.

Conductance measurements with A Type-RC Conductivity Bridge of dispersions of gum guar and polyoxyethylene glycol, establish the presence of the hydrogen-bonded chelation compound formation. The formation of the new hydrogen-bonded chelation compound is demonstrated through the measurement of the conductance of the product of the reaction of gum guar and polyoxyethylene glycol with the unexpected finding that this value is less than the sum of the conductance of the individual moieties. The conductance for a mixture of gum guar and polyoxyethylene glycol in which there is no hydrogen-bonded chelation complex compound formation would be expected to be the sum of the individual conductance measurements for the separate components of the mixture. Thus, we find that the resistance determined for gum guar at 1 percent concentration and at pH 5.55, is 1225 ohms and the conductance value is $808 \text{ mhos} \times 10^6$. The conductance determined for polyoxyethylene glycol, having an average molecular weight of 400, and which is known in the trade as "Carbowax 400," at 1 percent concentration and pH 6.15, has a resistance of 17,300 ohms and a conductance of $57.5 \text{ mhos} \times 10^6$. The hydrogen-bonded chelation compound formed by gum guar and polyoxyethylene glycol-400 at the same concentration, has a pH of 5.95, has an average resistance of 1420 ± 30 ohms and

an average conductance of $705 \pm 15 \text{ mhos} \times 10^6$. The values determined are reproducible and characteristic for the particular hydrogen-bonded chelation compound formed. When larger molecular weight polyoxyethylene glycol compounds are used as reagents, such as polyoxyethylene glycol 4,000, the degree of hydrogen-bonded formation is lessened, so that, for example, the conductance for the chelation compound of gum guar-polyoxyethylene glycol 4000 has a conductance of $795 \text{ mhos} \times 10^6$. If hydrogen-bonded chelation compound formation has not occurred, then the conductance for the mixture would be $865.5 \text{ mhos} \times 10^6$.

When a suppository prepared with this new compound is inserted into the body, the hydrophilic character of the base causes it to absorb moisture, producing a uniform disintegration and dispersion of the suppository. The resultant increases surface area of the dispersed hydrophilic materials coats the hydrophilic ano-rectal mucosa to provide intimate contact with the tissue barrier, thereby facilitating absorption for those substances that tended to enter the systemic circulation or, to permit the full therapeutic activity for those agents intended to exert a local effect. Thus, there is no pooling of the suppository ingredients as would occur when hydrophobic suppository materials are used, nor is there a dependence upon large amounts of water to cause disintegration when hydrophilic compositions are used. This unique effect is achieved because of the desirable coefficient of expansion of the hydrogen-bonded chelation compound which results in a surface shearing action which produces a rapid disintegration of the suppository. This effect is independent of the melting point of the compound and is initiated with only minimal amounts of moisture. The unique physical characteristics of the hydrogen-bonded chelation suppository compound permits high pressure rapid molding without surface liquefaction and does not require additive stabilizers or lubricants to facilitate the ejection of the formed suppository from the mold. When the hot pour technique is used, the high viscosity of the suppository mass retards sedimentation so that a uniform dispersion is maintained even in the liquid state. The new suppository compound does not turn rancid and is stable under the ordinary conditions of storage.

The new suppository base is non-irritating to the ano-rectal mucosa and may be introduced even in the immediate post-operative period.

In order to form the new suppository chelation compound, the selected polycyclohexose compound is mixed with the polyoxyethylene glycol and the mixture warmed to a temperature of between 50°C . and 65°C ., for a period of at least 15 minutes. While the lower temperature range of 40°C . may be used for the lower molecular weight polyoxyethylene glycols, as for example, those polyoxyethylene glycols having a molecular weight of from 200 to 600, the upper temperature range of 65°C . is utilized for those members of the polyoxyethylene glycols series having a molecular weight of from 1000 to 6000. During the warming phase, the mixture is stirred so that a uniform distribution of the polycyclohexose compound in the polyoxyethylene glycol is achieved. After the desired warming period is ended, the stirring is continued while the compound is allowed to cool. After cooling to room temperature, a plastic, solid, chelation compound results which may be readily shaped into the desired suppository and which is readily dispersible in aqueous fluids.

The ratio of polycyclohexose compound to polyoxyethylene compound required to form the desired hydrogen-bonded chelation compound ranges from 5 parts by weight of the polycyclohexose and 95 parts by weight of the polyoxyethylene glycol, to 40 parts by weight of the polycyclohexose to 60 parts by weight of the polyoxyethylene glycol. A preferred range of ratio concentration of the components is between 10 parts to 25 parts by weight of the polycyclohexose to 90 parts to 75 parts by weight

of the polyoxyethylene glycol. The exact ratio of components selected to form the new hydrogen-bonded chelation compound suppository base depends upon the particular intended use of the suppository and its manufacturing technique to be employed. Thus, a suppository intended to be manufactured by high speed compression apparatus, will require a higher degree of hydrogen-bonding to withstand the increased pressures and stresses and consequently the upper limits of range of the ratio of concentration of components will be used. Similarly, when the hot pour technique is to be utilized for a suppository containing appreciable quantities of suspended active ingredients, the upper concentrations will be preferred because of the increased viscosity of the molten new suppository compound. When a preparation is intended as a carrier for medication to be utilized in pediatric practice, the lower ranges of the ratio of concentration of components are more desirable to derive a more pliable suppository mass.

When it is desired to utilize this new suppository base material for the manufacture of pharmaceutically acceptable suppositories, the appropriate quantity of prepared new suppository compound is placed in a suitable container and melted over a water bath. Should it be preferred to utilize the dry composition, then the solid suppository compound is subdivided into coarse granular particles, either by passing through a comminuting apparatus or by trituration. The pharmacologically active material is then added to the suppository base whether molten or shredded and is uniformly dispersed. The suppositories are then manufactured either by compression-extrusion or through molding by the hot pour technique.

Examples of drugs which may be incorporated with the suppository base and then shaped into suppositories of suitable size for therapeutic administration are, antibiotics, as for example, tetracycline, penicillin, chlortetracycline, neomycin, bacitracin, polymyxin and the sulfa drugs; antiseptic agents; germicides; contraceptive agents; hormones, such as testosterone, estrone, hexesterol, stilbestrol, thyroid hormone, thyroid substance, thyroxine; the steroids, such as hydrocortisone, cortisone-alcohol, prednisolone; analeptic agents, such as caffeine, theophyllin and metrazole; diuretic compounds such as chlorthiazine, hydrochlorthiazine, fluoromethiazine; sedative agents, such as barbituric acid derivatives, hydantoin, derivatives, central nervous system stimulants, such as amphetamine; analgesic medication such as aspirin, choline salicylate, calcium salicylate, N-methylglucammonium salicylate, betaine salicylate, aceopheneditin, phenylbutazone, and laxative medications such as phenolphthalein, emodin, isatin, senna, cascara and extracts of these; cardio-tonic agents, such as digitalis, ouabain and quinidine salts and the narcotic medications, including the opium derivatives. The concentration of these therapeutic agents to be used in the suppository base is the full therapeutic dosage which is used in therapy, since there is no interference with the pharmacologic action by the new suppository base compound.

The following examples illustrate the scope of this invention.

Example 1

In a suitable container is placed 400 gms. of polyoxyethylene glycol-400 and 600 gms. of polyoxyethylene glycol-1000. The mixture is warmed to about 50° C., until complete solution is achieved and then 1 kilogram of polyoxyethylene glycol-6000 is added in small increments to the warm solution. When all of the polyoxyethylene glycol-6000 has been added, the mixture is stirred while 200 gms. of gum guar is added in small increments with stirring. After all of the gum guar has been added, the stirring is continued while the reaction mixture is warmed at a temperature of between 55° and 65° C. for one-half hour, after which time it is allowed to cool to room temperature. Upon cooling a cream colored waxy solid is obtained which has a melting point of 57°-59° C. A 2

gm. sample is completely dispersed in 20 ml. of water within 20 minutes at 37° C. Although the melting point of the compound is between 57° and 59° C., it may be molded at a temperature of 45° C. During the molding operation for the preparation of suppositories, the new base assumes a rigid form within one minute. When high speed compression molding procedures are used to form suppositories, the new compound may be worked with at temperature range of from room temperature to as high as 50° C. It will be found that the suppositories are ejected rapidly and smoothly, and without sticking to the die.

The hardness of the suppository is determined by the extent of hydrogen-bond formation between the polycyclohexose compound and the polyoxyethylene glycol. Thus, the range in concentration for the different molecular weight polyoxyethylene glycol compounds may vary with the desired texture of the suppository, while the hardness will depend directly upon the degree of hydrogen-bonded chelation linkage present.

Example 2

In a suitable container is placed 1600 gms. of polyoxyethylene glycol-400 and to this is added 600 gms. of gum guar. The mixture is warmed to about 50° C. and stirred for a period of one-half hour, after which time it is allowed to cool to room temperature. Upon cooling the compound becomes a creamy, waxy, solid having a melting point of 50° C. to 53° C. It has a complete dispersion in water at 37° C. within 20 minutes. The conductance of a 1 percent concentration at pH 5.95, is 705 ± 15 mhos $\times 10^6$. This conductance value establishes that hydrogen-bonding occurs since the conductance for the new compound is less than the sum of the conductance values for the separate, individual components. Gum guar has a conductance of $808 \text{ mhos} \times 10^6$ and polyoxyethylene glycol-400 has a conductance of $46.5 \text{ mhos} \times 10^6$.

Example 3

In a suitable container is placed 700 gms. of polyoxyethylene glycol-4000 and 300 gms. of gum guar. The mixture is warmed to a temperature of 60° C. which is maintained over a period of 1 hour, with constant stirring. At the end of this time, the heating is stopped and the molten material is allowed to cool to room temperature. While cooling a hard, solid mass results which has a melting point of from 61°-63° C. A 2 gram sample shows complete dispersion in 20 ml. of water, at 37° C. within 20 minutes. The pH of a 1 percent dispersion is 6.02 and it shows a conductance of $795 \text{ mhos} \times 10^6$.

Example 4

In place of the gum guar described in Examples 1 through 3 above, there may be substituted in equal quantities, algin, pectin and carboxymethylcellulose. The remainder of the steps being the same.

Example 5

In place of the polyoxyethylene glycol-400, polyoxyethylene glycol-1000, and polyoxyethylene glycol-6000 described in Examples 1 through 4 above, there may be substituted wholly, or in part, a polyoxyethylene glycol having a molecular weight range within 200 and 6000. The particular polyoxyethylene glycol to be used depends upon the desired texture in the finished suppository. When larger amounts of a lower molecular weight polyoxyethylene glycol are used, then the texture of the finished suppository will be more wax-like. Such a suppository will be less friable and may be prepared in long, narrow, rod-like shapes. The exact amount of each of the particular polyoxyethylene glycol to be used will depend upon the particular purpose and method of manufacture for the suppository.

The formation of the hydrogen-bonded chelation compound occurs more readily with the lower molecular weight polyoxyethylene glycol compounds than with the

higher molecular weight compounds. However, in all instances, hydrogen-bonded chelation compound formation may be shown through the measurement of the conductance value for the new compound formed. The hydrogen bonding between the gum guar and the polyoxyethylene glycol is clearly established by the unexpected finding of a conductance which is less than the sum of the separate conductance of the individual components. The remainder of the steps being the same.

Example 6

To 100 gms. of a compound prepared according to the method described in Examples 1 through 5 above, and which has been melted on a water-bath, at a temperature below 65° C., is added 15 gms. of powdered aspirin, U.S.P. The aspirin should be subdivided to at least 120 standard mesh particle size, prior to adding to the molten base. The mixture is stirred to achieve uniform distribution of the aspirin and then removed from the water-bath to cool to room temperature. When the whole has solidified, the mixture is chilled and passed through a Number 8 standard mesh screen. The powdered suppository material is then filled into a compression-extrusion apparatus fitted with a suitable mold, so that suppositories weighing 2 gm. each may be prepared. Should it be desired to use a hot pour molding technique, for the preparation of suppositories, then the molten mass is poured directly into the mold and allowed to cool therein. A mold of sufficient size and shape to prepare a 2 gm. suppository is utilized. The suppositories are administered from 1 to six times daily, depending upon the needs of the patient.

Example 7

In place of aspirin used in Example 6 above, there may be substituted any of the following therapeutic compounds, or mixtures of these, as well as other compatible active therapeutic compounds, so that the concentration of the therapeutic agent, per suppository, will be within the active therapeutic range, as for example, the range described for each of the compounds noted below.

Active agent:	Range of concentration per suppository
Erythromycin	100 to 250
Penicillin	200 to 500
Tetracycline	100 to 250
Oxytetracycline	100 to 250
Chlortetracycline	100 to 250
Piperazine citrate	100 to 250
Pyrillamine malleate	25 to 50
Promethazine hydrochloride	10 to 50
Pheniramine malleate	5 to 25
Sulfanilamide	100 to 500
Sulfathiazole	100 to 500
Sulfamerzine	100 to 500
Sulfacetamide	100 to 500
Phthallyl sulfathiazole	100 to 500
Amphetamine sulfate	5 to 15
Cyclopentamine hydrochloride	15 to 25
Isoxsuprine hydrochloride	5 to 10
Butabarbital	15 to 60
Phenobarbital	15 to 60
Secobarbital	15 to 60
Pentobarbital	15 to 60
Chlorpromazine	25 to 100
Fluphenazine	0.25 to 5
Mepazine	25 to 100
Promazine	10 to 200
Desoxycorticosterone acetate	25 to 50
Cortisone acetate	5 to 25
Dexamethasone	0.5 to 1
Hydrocortisone cyclopentyl propionate	5 to 25
Prednisolone acetate	5 to 25
Estradiol	0.1 to 1.0
Dienestrol	0.1 to 10

Active agent:	Range of concentration per suppository
Diethylstilbestrol	0.5 to 10
Hexestrol	0.5 to 5
Methyltestosterone	5 to 25
Sodium levothyroxine	0.1 to 5
Sodium liothyronine	5 to 50
Digitoxin	0.1 to 0.2
Gitoxin	0.1 to 0.2
Digitalis powder	100 to 200
Quinidine sulfate	200 to 400
Quinidine polygalacturonate	200 to 300
Quinidine gluconate	200 to 300
Quinidine galacturonate	200 to 300
N-methylglucammonium salicylate	50 to 300
Choline salicylate	50 to 300
Phenacetin	50 to 300
Caffeine	5 to 30
Ephedrine	5 to 30
Theophyllin	5 to 30
Senna	5 to 300
Cascara	25 to 100
Isatin	5 to 15

Suppositories prepared with these and other therapeutic agents, which are pharmaceutically suitable for suppository administration, are stable and will result in the full desired therapeutic effect for the respective active ingredients. Such suppositories are administered from 1 to 6 times daily, depending upon the need of the patient, the pharmacologic effects of the active ingredient and the status of the disease present.

Suppositories prepared according to the procedures described above are a desirable means of administering pharmacologically active materials. It will be found that these are completely dispersible in minimal quantities of aqueous fluid, usually within a period of 20 minutes, at body temperature, notwithstanding that the melting point of the base is higher than body temperature. The dispersion of the suppository is achieved through a unique action. When the suppository is introduced into the body cavity the hydrophilic properties of the base adsorbs moisture, causing a unilateral swelling action. The expansion of the hydrogen-bonded polycyclohexose moiety facilitates the uniform dispersion of the suppository base and the active ingredient. The hydrophilic character of the suppository base tends to aid adherence of the dispersed substances as a surface film on the mucosal wall of the body cavity. This intimate contact promotes the rapid transfer and absorption of pharmacologically active material. In the instances where the pharmacologically active material does not traverse the mucosal tissue, then the intimate tissue contact provided by such uniform dispersion of the suppository base and active ingredient, results in a superior local therapeutic effect.

Example 8

Suppositories prepared from a compound obtained as a result of Examples 1 through 5 above, may be used to induce laxation or to provide an emollient coating to the ano-rectal mucosa. When it is desired to utilize the suppository materials in such manner, then the suppository mass is shaped into suppositories, having an average weight of from 0.50 gm. to 2.0 gms. each. The suppositories may be manufactured by either the cold compression-extrusion technique or the hot pour method. Such suppositories may be inserted into the rectum from 1 to 4 times daily, depending upon the particular patient need. In instances where a lubricant effect is desired, to induce laxation, the use may be at morning and night. When a protective effect to the ano-rectal mucosa is desired, then a more frequent usage is indicated and the suppository may be inserted up to 4 times daily.

What is claimed is:

1. A suppository comprising a hydrogen-bonded chelation compound formation containing from 5 to 40 parts by weight of a polymeric polycyclohexose compound selected from the group consisting of gum guar, pectin, algin, carboxymethylcellulose and mixtures of these; from 5 to 60 parts by weight of a polyoxyethyleneglycol compound selected from the group consisting of polyoxyethylene glycols having a molecular weight of from 200 to 6000 and mixtures of these, and a therapeutically sufficient quantity of a therapeutically active compound, selected from the group consisting of erythromycin, penicillin, tetracycline, oxytetracycline, chlortetracycline, piperazine citrate, pyrimidine maleate, promethazine hydrochloride, pheniramine maleate, sulfanilamide, sulfathiazole, sulfamerazine, sulfacetamide, phthalyl sulfathiazole, amphetamine sulfate, cyclopentamine hydrochloride, isoxsuprine hydrochloride, butabarbital, phenobarbital, secobarbital, pentobarbital, chlorpromazine, fluphenazine, mepazine, promazine, desoxycorticosterone acetate, cortisone acetate, dexamethasone, hydrocortisone cyclopentyl propionate, prednisolone acetate, estradiol, dienestrol, diethylstilbestrol, hexestrol, methyltestosterone, sodium levothyroxin, sodium liothyronine, digitoxin, gitoxin, digitalis powder, quinidine sulfate, quinidine polygalacturonate, quinidine gluconate, quinidine galacturonate, N-methylglucammonium salicylate, choline salicylate, acetylsalicylic acid, phenacetin, caffeine, ephedrine, theophyllin, senna cascara, isatin, and mixtures of these.

2. A suppository as described in claim 1, said therapeutically active compound being from 5 mg. to 15 mg. of isatin.

3. A suppository as described in claim 1, said therapeutically active compound being from 25 mg. to 100 mg. of cascara sagra.

4. A suppository as described in claim 1, said therapeutically active compound being from 5 mg. to 30 mg. of theophyllin.

5. A suppository as described in claim 1, said therapeutically active compound being from 10 mg. to 200 mg. of Promazine.

6. A suppository as described in claim 1, said therapeutically active compound being from 5 mg. to 25 mg. of cortisone acetate.

7. A suppository as described in claim 1, said therapeutically active compound being from 5 mg. to 300 mg. of senna.

8. A suppository as described in claim 1, said therapeutically active compound being from 100 to 250 mg. of tetracycline.

9. The method of causing an elevated blood level of aspirin which comprises the step of inserting into a body cavity a suppository described in claim 1, said therapeutically active compound being aspirin.

10. The method of causing an elevated blood level of choline salicylate which comprises the step of inserting into a body cavity a suppository described in claim 2, said therapeutically active compound being choline salicylate.

11. The method of causing an elevated blood level of promazine which comprises the step of inserting into a body cavity a suppository described in claim 1, said therapeutically active compound being promazine.

12. The method of causing an elevated blood level of

ephedrine which comprises the step of inserting into a body cavity a suppository described in claim 1, said therapeutically active compound being ephedrine.

13. The method of causing an elevated blood level of theophyllin which comprises the step of inserting into a body cavity a suppository described in claim 2, said therapeutically active compound being theophyllin.

14. The method of causing an anorectal lubricant mucosal film which comprises the step of inserting into the rectum a suppository comprising a hydrogen-bonded chelation compound formation containing from 5 to 40 parts by weight of a polymeric polycyclohexose compound selected from the group consisting of gum guar, pectin, algin, carboxymethylcellulose and mixtures of these; and from 95 to 60 parts by weight of a polyoxyethyleneglycol selected from the group consisting of polyoxyethylene glycols with a molecular weight of from 200 to 6000, and mixtures of these.

15. The method for achieving a laxative action which comprises the step of inserting into a body cavity a suppository comprising a hydrogen-bonded chelation compound formation containing from 5 to 40 parts by weight of a polymeric polycyclohexose compound selected from the group consisting of gum guar, algin, pectin carboxymethylcellulose and mixtures of these, and from 95 to 60 parts by weight of a polyoxyethyleneglycol compound selected from the group consisting of polyoxyethylene glycols having a molecular weight of from 200 to 6000 and mixtures of these.

16. A method for achieving a laxative action which comprises the step of inserting into a body cavity a chelate compound suppository of claim 1, said therapeutically active compound being selected from the group consisting of isatin, cascara sagra, senna and extracts of these.

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