Vaginal suppository

This invention relates to a vaginal composition useful as an agent for contraception. In particular the invention relates to a vaginal suppository useful for contraception purposes which comprises a spermicide, a suppository base, a foaming agent and a foam-stabilizing agent.

The use of spermicidal substances such as suppositories, effervescent tablets and foams for local contraception is well known in the art. U.S. Patent No. 2,854,377 describes nontoxic pharmaceutical compositions which effervesce on contact with moisture. In the latter patent, surface active materials are added to conventional mixtures used to produce carbon dioxide for the purpose of creating more stable foams with smaller bubbles. U.S. Patent No. 3,062,715 describes a vaginal tablet comprising effervescent powder and rubber substances which effect a rapid decomposition of the tablets and hence a rapid dissolution of the tablet. German Patent No. 893,997 describes vaginal ovulae consisting of a wax-type carrier and a spermicide. After melting, the carrier, together with the aqueous body fluids, forms a tenacious emulsion of the oil-in-water type. However, the spermicide is not distributed homogeneously in the emulsion. U.S. Patent No. 3,876,757 (equivalent of FR 2177019) relates to an improvement in a composition comprising a spermicide, a water-soluble polyethylene glycol which melts at body temperature and a mixture of substances which produce carbon dioxide with water and a foam stabilizer. However, this composition apparently does not produce a homogeneous mixture unless the specified ratio of ingredients is employed.

Foam aerosols consisting of readily-prepared foams are also known in the art. However, foams of this type are difficult to handle. Dosing and introduction tubes are required for application of the foam, and if too little foam is used, the protective effect is correspondingly diminished.

The known means of local contraception, therefore, are not entirely satisfactory. There is a need for a contraceptive agent which can be easily introduced into the vagina and which will safely provide a sufficient amount of the spermicide at all times, even when the volume of the natural body fluids present in the vagina is low.

The present invention relates to a contraceptive composition comprising a spermicide, a foaming agent, a foam-stabilizing agent and a water-soluble suppository base. Contraception is achieved by a diffusion of the spermicide throughout the vaginal cavity due to the foaming action which occurs as a result of direct contact between the suppository and the vaginal fluid. The foaming suppository of the present invention rapidly develops its full effectiveness in a matter of minutes after application and maintains its effectiveness over a long period of time. The unique combination of ingredients results in a homogenous composition which is capable of distributing the spermicide throughout the vaginal cavity.

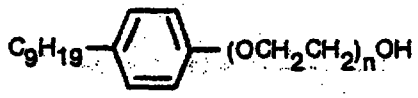
According to the present invention, a mixture of water-soluble polyethylene glycols is employed as the suppository base. The mixture preferably comprises a polyethylene glycol having a molecular weight of between about 1000 and 1200 and a second polyethylene glycol having a molecular weight of between about 1300 and 1600. The preferred mixture is a polyethylene glycol having a molecular weight of about 1000 and a polyethylene glycol having a molecular weight of about 1540. The mixture of glycols is present in a ratio of about 75—80% for the lower molecular weight polymer and about 3—5% for the higher molecular weight polymer.

As the foaming agent it is preferred to use a mixture of a water-soluble organic acid such as citric acid, tartaric acid and succinic acid and an alkaline or alkaline earth carbonate or bicarbonate such as sodium bicarbonate, sodium carbonate and potassium carbonate, for example. The preferred mixture is comprised of citric acid and sodium bicarbonate. The foaming agent is present in a ratio of from about 5—7%. The preferred ratio is about 2% of the acid component and about 4% of the basic salt. Although a lower ratio of the foaming agent is employed in the present invention than in the prior art suppositories, the foaming agent yields sufficient carbon dioxide development to effect a thorough diffusion of the spermicide in the vaginal cavity. Thus a smaller evolution of gas and a lower increase in temperature occur which results in fewer of the side effects generally associated with effervescent supporitories of this type. The mixture provides a system having a pH between about 4.5 and 7.5.

A mixture of foam-stabilizing agents is added to assure even development of the foam as well as uniformity and consistency over an extended period of time. As the foam-stabilizing agent a mixture of an amphoteric organic surfactant and a water-soluble film-forming agent is employed. The organic surfactant serves as a foam stabilizer and in addition tends to reduce the irritation commonly associated with compositions of this type. The film-forming agent serves as a support or binding agent for the foam after it is produced. The film-forming agent also increases the viscosity of the fluid in the vaginal cavity resulting in an increased barrier effect for the suppository. Amphoteric surface-active agents which can be employed include Amphoteric-1*, Amphoteric-2*, Amphoteric-5*, Amphoteric-6*, Amphoteric-9*, Amphoteric-10*, Amphoteric-14*, Amphoteric-19*, and Amphoteric-20* (sold by Miranol Chemical Co., Inc.), Monateric CA*, Monateric CSH—32*, Monateric ISA—35*, Monateric CM—365*, Monateric 805* and Monateric CAB* (sold by Mona Industries, Inc.). The preferred surface-active agent is Amphoteric-19*. As the film-forming agent Povidone K26—28*, Povidone K29—32 (sold by General Aniline & Film Corp.), Cellulose gum, Hydroxyethylcellulose, Cellulose ether and Reten 205* (sold by Hercules Powder Co.), and sodium-alginate may be employed. The preferred film-forming agent is Providone K29—32* (polyvinylpyrrolidone). The mixture of foam stabilizing agents is

employed in a ratio from about 4—10%. The preferred mixture is about 2% of the surface active agent and about 5% of the film-forming agent.

As the spermicide it is preferred to use an alkylphenoxyethoxyethanol of the formula



wherein n is an integer from 5—12. The preferred spermicide is a nonylphenoxypolyethoxyethanol wherein n is 9, commonly known as nonoxynol-9. The spermicide distributes itself homogeneously in the foam as it forms and the foam and spermicide are distributed equally and evenly over the entire vaginal cavity as the foam develops. The spermicide is present in a ratio of from about 2—7%. In a preferred embodiment about 5—6% of the spermicide is employed.

Although the contraceptive composition of the present invention may be prepared in a variety of shapes, it is preferred to use a torpedo-shaped suppository having a smooth surface appearance. The suppository has a weight between about 1.6 and 2 grams. The preferred weight is about 1.8 grams. The suppository is prepared by adding the spermicide to a heated mixture of the polyethylene glycols with stirring until a clear solution is obtained. The amphoteric surfactant is added to the clear solution followed by the addition of the organic acid. The film-forming agent is then added to the mixture and the mixing is continued until a uniform mixture is obtained. The alkali or alkaline earth metal carbonate is then added and the mixture is poured into the suppository shell and revolved until it solidifies. A more detailed description of the process according to the invention is described in Example I.

Example I

A mixture of a polyethylene glycol having a molecular weight of about 1000 (1395 mg) and a polyethylene glycol having a molecular weight of about 1540 (71.0 mg) is heated at 52—62°C with constant mixing until a clear solution is obtained. Nonoxynol-9 (100 mg) is added and the stirring is continued. The temperature is adjusted to 52—62°C and Amphoteric-19* (26 mg) is added with stirring. The stirring is continued until a clear solution is obtained after which anhydrous citric acid (40.5 mg) is added with stirring. The stirring is continued until the citric acid dissolves after which Povidone K29—32* (90 mg) is added with stirring. The temperature of the mixture is adjusted to 52—62°C and the stirring is continued until a uniform suspension is formed. The mixture is cooled to 43—47°C after which sodium bicarbonate (47.5 mg) is added with stirring. The mixture is stirred at 43—47°C for 20 minutes after which it is poured into a suppository shell.

The suppository prepared by the above process has the following composition:

Ingredient	Percent	wt. (grams)
nonoxynol-9	5.56	0.1000
Amphoteric-19*	2.00	0.0360
Povidone*	5.0	0.0900
citric acid, anhydrous	2.25	0.0405
sodium bicarbonate	3.75	0.0675
polyethylene glycol 1000	77.50	1.3950
polyethylene glycol 1540	3.94	0.0710
	100.00%	1.8000 g

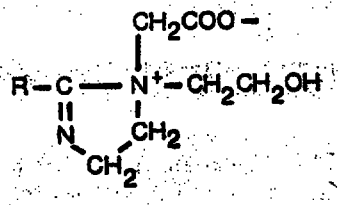
The suppository dissolves completely in about 1 ml of water in about 10 minutes at a temperature of about 37°C. Upon contact with the water, a slight development of foam starts with simultaneous dissolution of the suppository. The foam development increases constantly until the dissolution is complete. The foam which forms shows fine pores, is even and remains as such over an extended period of time.

The above example is provided by way of illustration and is not intended to limit the scope of the present invention, the scope of which is defined by the appended claims.

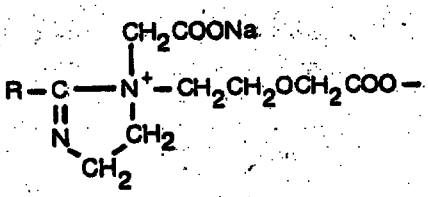
The names marked with an asterisk are Trade marks.

Reten 205* is a cationic water-soluble polymer

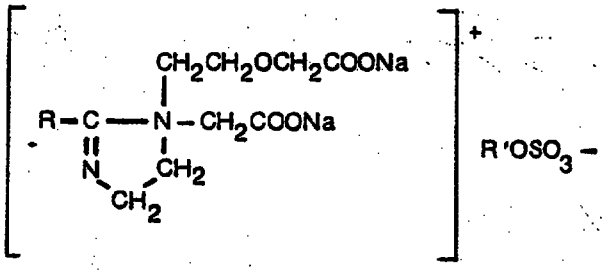
Amphoteric-1 is a long chain imidazoline type of zwitterion which conforms generally to the formula



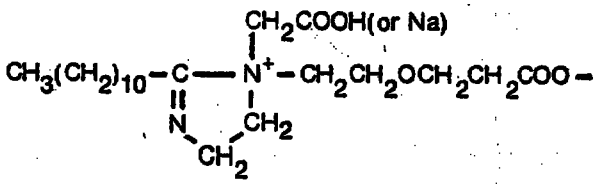
where R is derived from the coconut fatty radical. Amphoteric-2* is a long chain imidazoline type of zwitterion which conforms generally to the formula



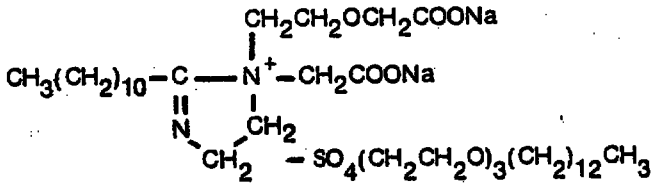
wherein R is derived from the coconut fatty radical. Amphoteric-5* is a long chain imidazoline type of zwitterion which is generally described as a sodium trideceth sulfate derivative of Amphoteric-2*. Amphoteric-6* is a long chain imidazoline type of zwitterion which is generally described as a sodium lauryl sulfate derivate of Amphoteric-2*. Amphoteric-9* is along chain imidazoline type of zwitterion which conforms generally to the formula



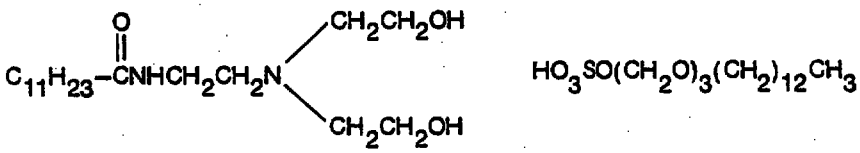
wherein R is derived from the coconut fatty radical and R' is derived from a mixture of lauryl and laureth-3 radicals. Amphoteric-10* is a long chain imidazoline type of zwitterion which conforms generally to the formula



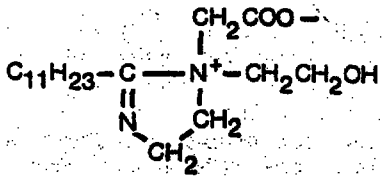
Amphoteric-14* is a long chain imidazoline type of zwitterion which conforms generally to the formula



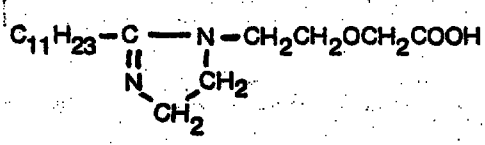
Amphoteric-19* is a long chain imidazoline type of zwitterion which conforms generally to the formula



Amphoteric-20* is a long chain imidazoline type of zwitterion which conforms generally to the formula

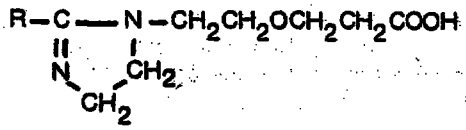


Monateric CA* (Amphoteric-11*) is the amphoteric organic compound that conforms generally to the formula



Monateric CSH—32* is a fully biodegradable amphoteric in the form of a 32% active sodium salt of a dicarboxymethyl fatty acid derived imidazoline.

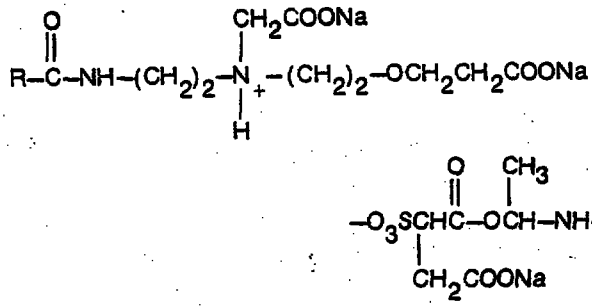
Monateric ISA—35* (Amphoteric-12*) is the amphoteric organic compound that conforms generally to the formula



wherein R is derived from isostearic acid.

Monateric CM—36S* is a coco-imidazoline based amphoteric.

Monateric 805* (Amphoteric-18*) is the amphoteric organic compound that conforms generally to the formula



and Monateric CAB* is a coco-amido betaine.

Claims

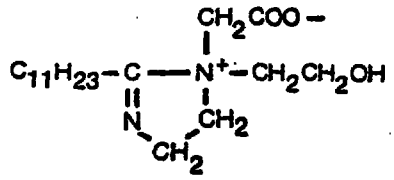
1. A spermicidally active vaginal suppository comprising 2—7% by weight of an alkylphenoxy-polyethoxyethanol as the spermicide, about 78—85% of a mixture of water-soluble polyethylene glycols as the suppository base, about 5—7% of a mixture of an organic acid and an inorganic bicarbonate as the foaming agent and about 4—10% of a mixture of an amphoteric surfactant and a water-soluble film-forming agent as the foam-stabilizing agent.

2. A spermicidally active vaginal suppository according to Claim 1 wherein the mixture of water-soluble polyethylene glycols consists of 75—80% of glycols having a molecular weight of between 1000 and 1200 and 3—5% of glycols having a molecular weight of between 1300 and 1600, said percentages being based on the weight of the suppository.

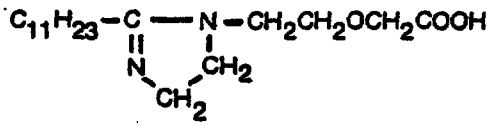
3. A spermicidally active vaginal suppository according to Claim 2 wherein the mixture of water-soluble polyethylene glycols consists of 75—80% of glycols having a molecular weight of about 1000 and 3—5% of glycols having a molecular weight of about 1540, said percentages being based on the weight of the suppository.

4. A spermicidally active vaginal suppository according to any one of claims 1 to 3 wherein the amphoteric surfactant is Amphoteric-19* and the water-soluble film-forming agent is polyvinylpyrrolidone.

5. A spermicidally active vaginal suppository according to Claim 1 comprising 5.5% by weight of an alkylphenoxypolyethoxyethanol as the spermicide, a mixture of 77.5% of a polyethylene glycol having a molecular weight of 1000 and 3.9% of a polyethylene glycol having a molecular weight of 1540 as the mixture of water-soluble polyethylene glycols, a mixture of 2.25% of an organic acid and

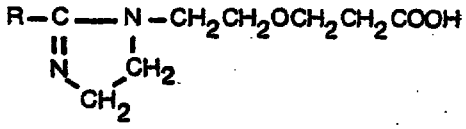


Monateric CA* (Amphoteric-11*) is the amphoteric organic compound that conforms generally to the formula



Monateric CSH—32* is a fully biodegradable amphoteric in the form of a 32% active sodium salt of a dicarboxymethyl fatty acid derived imidazoline.

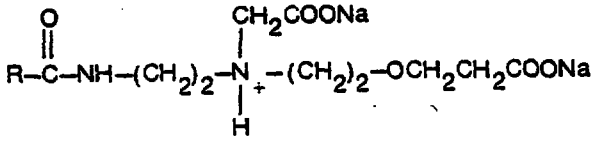
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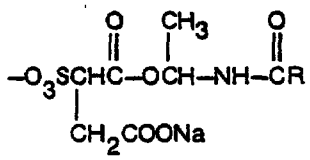


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and Monateric CAB* is a coco-amido betaine.

Claims

1. A spermicidally active vaginal suppository comprising 2—7% by weight of an alkylphenoxy-polyethoxyethanol as the spermicide, about 78—85% of a mixture of water-soluble polyethylene glycols as the suppository base, about 5—7% of a mixture of an organic acid and an inorganic bicarbonate as the foaming agent and about 4—10% of a mixture of an amphoteric surfactant and a water-soluble film-forming agent as the foam-stabilizing agent.

2. A spermicidally active vaginal suppository according to Claim 1 wherein the mixture of water-soluble polyethylene glycols consists of 75—80% of glycols having a molecular weight of between 1000 and 1200 and 3—5% of glycols having a molecular weight of between 1300 and 1600, said percentages being based on the weight of the suppository.

3. A spermicidally active vaginal suppository according to Claim 2 wherein the mixture of water-soluble polyethylene glycols consists of 75—80% of glycols having a molecular weight of about 1000 and 3—5% of glycols having a molecular weight of about 1540, said percentages being based on the weight of the suppository.

4. A spermicidally active vaginal suppository according to any one of claims 1 to 3 wherein the amphoteric surfactant is Amphoteric-19* and the water-soluble film-forming agent is polyvinylpyrrolidone.

5. A spermicidally active vaginal suppository according to Claim 1 comprising 5.5% by weight of an alkylphenoxypolyethoxyethanol as the spermicide, a mixture of 77.5% of a polyethylene glycol having a molecular weight of 1000 and 3.9% of a polyethylene glycol having a molecular weight of 1540 as the mixture of water-soluble polyethylene glycols, a mixture of 2.25% of an organic acid and

3.75% of an inorganic bicarbonate as the foaming agent and a mixture of 5% of polyvinylpyrrolidone as the film-forming agent and 2% of an amphoteric surfactant as the foam stabilizer.

6. A spermicidally active vaginal suppository according to any one of claims 1 to 5 wherein the alkylphenoxypolyethoxyethanol is p-nonylphenoxypolyethoxyethanol.

7. A spermicidally active vaginal suppository according to any one of claims 1 to 6 wherein the organic acid is citric acid, tartaric acid or succinic acid and the inorganic bicarbonate is sodium bicarbonate or potassium bicarbonate.

8. A spermicidally active vaginal suppository according to Claim 7 wherein the organic acid is citric acid and the inorganic bicarbonate is sodium bicarbonate.

9. A method of preparing a spermicidally active vaginal suppository according to any one of claims 1 to 8, comprising:

adding, to a heated mixture of the polyethylene glycols, the spermicide, the amphoteric surfactant, the organic acid, the water-soluble film-forming agent and the inorganic bicarbonate;

pouring the mixture into a suppository shell; and

allowing the mixture to solidify to form the suppository.

Revendications

1. Suppositoire vaginal actif comme spermicide comprenant environ 2 à 7% en poids d'un alcoylphénoxypolyéthoxyéthanol comme spermicide, environ 78—85% d'un mélange de polyéthylèneglycols solubles dans l'eau comme base suppositoire, environ 5—7% d'un mélange d'un acide organique et d'un bicarbonate inorganique comme agent moussant et environ 4—10% d'un mélange d'un agent tensio-actif amphotère et d'un agent formant pellicule soluble dans l'eau comme agent stabilisateur de mousse.

2. Suppositoire vaginal actif comme spermicide selon la revendication 1 où le mélange de polyéthylèneglycols solubles dans l'eau se compose de 75—80% de glycols ayant un poids moléculaire compris entre 1000 et 1200 et de 3 à 5% de glycols ayant un poids moleculaire compris entre 1300 et 1600, lesdits pourcentages étant basés sur le poids du suppositoire.

3. Suppositoire vaginal actif comme spermicide selon la revendication 2 où le mélange de polyéthylèneglycols solubles dans l'eau se compose de 75—80% de glycols ayant un poids moléculaire d'environ 1000 et de 3—5% de glycols ayant un poids moléculaire d'environ 1540, lesdits pourcentages étant basés sur le poids du suppositoire.

4. Suppositoire vaginal actif comme spermicide selon l'une quelconque des revendications 1 à 3 où l'agent tensio-actif amphotère est Amphoteric-19* et l'agent formant pellicule soluble dans l'eau est la polyvinylpyrrolidone.

5. Suppositoire vaginal actif comme spermicide selon la revendication 1 comprenant 5,5% en poids d'un alcoylphénoxypolyéthoxyéthanol comme spermicide, un mélange de 77,5% d'un polyéthylèneglycol ayant un poids moléculaire de 1000 et 3,9% d'un polyéthylèneglycol ayant un poids moléculaire de 1540 comme mélange de polyéthylèneglycols solubles dans l'eau, un mélange de 2,25% d'un acide organique et 3,75% d'un bicarbonate inorganique comme agent moussant et un mélange de 5% de polyvinylpyrrolidone comme agent formant pellicule et 2% d'un agent tensio-actif amphotère comme stabilisateur de mousse.

6. Suppositoire vaginal actif comme spermicide selon l'une quelconque des revendications 1 à 5 où l'alcoylphénoxypolyéthoxyéthanol est le p-nonylphénoxypolyéthoxyéthanol.

7. Suppositoire vaginal actif comme spermicide selon l'une quelconque des revendications 1 à 6 où l'acide organique est l'acide citrique, l'acide tartrique ou l'acide succinique et le bicarbonate inorganique est le bicarbonate de sodium ou le bicarbonate de potassium.

8. Suppositoire vaginal actif comme spermicide selon la revendication 7 où l'acide organique est l'acide citrique et le bicarbonate inorganique et le bicarbonate de sodium.

9. Procédé de préparation d'un suppositoire vaginal actif comme spermicide selon l'une quelconque des revendications 1 à 8 dans lequel:

on ajoute, à un mélange chauffé des polyéthylèneglycols, le spermicide, l'agent tensio-actif amphotère, l'acide organique, l'agent formant pellicule soluble dans l'eau et le bicarbonate inorganique;

on verse le mélange dans une enveloppe de suppositoire; et

on laisse le mélange se solidifier pour former le suppositoire.

Patentansprüche

1. Ein spermizid wirksames Vaginalzäpfchen, enthaltend etwa 2 bis 7 Gew.-% eines Alkylphenoxypolyethoxyethanols als das Spermizid, etwa 78 bis 85% eines Gemisches von wasserlöslichen Polyethylenglycolen als die Suppositorienbasis, etwa 5 bis 7% eines Gemisches aus einer organischen Säure und einem anorganischen Bicarbonat als das schaumbildende Mittel und etwa 4 bis 10% eines Gemisches aus einem amphoteren oberflächenaktiven Mittel und einem wasserlöslichen filmbildenden Mittel als das schaumstabilisierende Mittel.

* C L M S *

2. Ein spermizid wirksames Vaginalzäpfchen gemäß Anspruch 1, worin das Gemisch aus wasserlöslichen Polyethylenglycolen aus 75 bis 80% von Glycolen mit einem Molekulargewicht von zwishen 1000 und 1200 und 3 bis 5% Glycolen mit einem Molekulargewicht von zwischen 1300 und 1600 besteht, welche Prozentsätze auf das Gewicht des Zäpfchens bezogen sind.

3. Ein spermizid wirksames Vaginalzäpfchen gemäß Anspruch 2, worin das Gemisch aus wasserlöslichen Polyethylenglycolen aus 75 bis 80% Glycolen mit einem Molekulargewicht von etwa 1000 und 3 bis 5% Glycolen mit einem Molekulargewicht von etwa 1540 besteht, welche Prozentsätze auf das Gewicht des Zäpfchens bezogen sind.

4. Ein spermizid wirksames Vaginalzäpfchen gemäß einem der Ansprüche 1 bis 3, worin das amphotere oberflächenaktive Mittel Amphoteric-19* ist und das wasserlösliche filmbildende Mittel Polyvinylpyrrolidon ist.

5. Ein spermizid wirksames Vaginalzäpfchen gemäß Anspruch 1, enthaltend 5,5 Gew.-% eines Alkylphenoxypolyethoxyethanols als das Spermizid, ein Gemisch aus 77,5% eines Polyethylenglycols mit einem Molekulargewicht von 1000 und 3,9% eines Polyethylenglycols mit einem Molekulargewicht von 1540 als das Gemisch aus wasserlöslichen Polyethylenglycolen, ein Gemisch aus 2,25% einer organischen Säure und 3,75% eines anorganischen Bicarbonats als das schaumbildende Mittel und ein Gemisch von 5% Polyvinylpyrrolidon als das filmbildende Mittel und 2% eines amphoteren oberflächenaktiven Mittels als das schaumstabilisierende Mittel.

6. Ein spermizid wirksames Vaginalzäpfchen gemäß einem der Ansprüche 1 bis 5, worin das Alkylphenoxypolyethoxyethanol p-Nonylphenoxypolyethoxyethanol ist.

7. Ein spermizid wirksames Vaginalzäpfchen gemäß einem der Ansprüche 1 bis 6, worin die organische Säure Zitronensäure, Weinsäure oder Bernsteinsäure ist und das anorganische Bicarbonat Natriumbicarbonat oder Kaliumbicarbonat ist.

8. Ein spermizid wirksames Vaginalsuppositorium gemäß Anspruch 7, worin die organische Säure Zitronensäure ist und das anorganische Bicarbonat Natriumbicarbonat ist.

9. Ein Verfahren zur Herstellung eines spermizid wirksamen Vaginalzäpfchens gemäß einem der Ansprüche 1 bis 8, umfassend:

Zusetzen zu einem erwärmten Gemisch der Polyethylenglycole des Spermizids, des amphoteren oberflächenaktiven Mittels, der organischen Säure, des wasserlöslichen filmbildenden Mittels und des anorganischen Bicarbonats;

Eingießen des Gemisches in eine Suppositorienform; und

Erstarrenlassen des Gemisches zur Ausbildung des Zäpfchens.