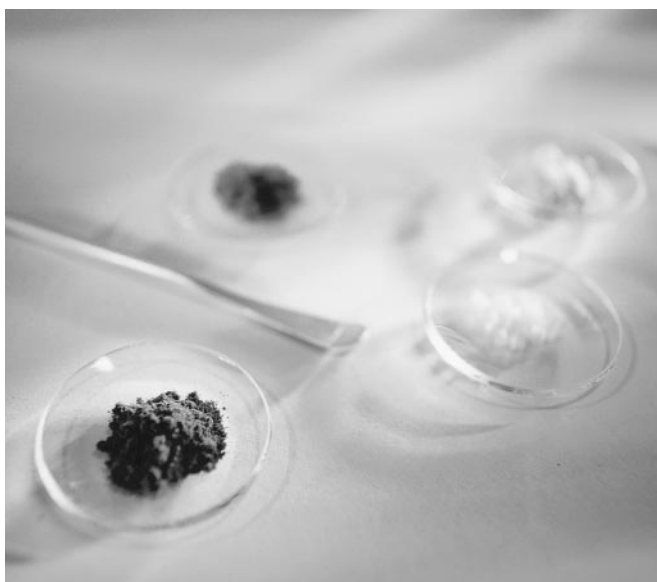


Compendium of Pharmaceutical Excipients for Vaginal Formulations

Sanjay Garg,* Kaustubh R. Tambwekar, Kavita Vermani, Alka Garg,
Chaman L. Kaul, and Lourens J. D. Zaneveld



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Development of an ideal vaginal formulation with desired characteristics in terms of safety, efficacy, patient compliance, aesthetics, acceptability to regulatory authorities, and cost requires a careful and meaningful selection of the active ingredients and excipients. This article lists all presently available vaginal excipients along with their functional categories, concentrations (where available), and regulatory status. The overall objective of this communication is to aid the formulation scientist in selecting the optimal excipients for the preparation of vaginal products.

Sanjay Garg is an assistant professor; Kaustubh R. Tambwekar is a PhD scholar; Kavita Vermani is a PhD scholar; and Chaman L. Kaul is director, all at the National Institute of Pharmaceutical Education and Research (NIPER), Sector 67, S.A.S. Nagar, Punjab-160062, India, tel. 91 172 214682; fax 91 172 214692, e-mail gargsanjay@yahoo.com. Alka Garg is a PhD scholar at the University Institute of Pharmaceutical Sciences, Panjab University, Chandigarh-160014, India, and Lourens J.D. Zaneveld is the director of the Program for Topical Prevention of Conception and Disease, Rush University, Chicago, IL.

*To whom all correspondence should be addressed.

Global research in pharmaceutical sciences will acquire new dimensions in the post-GATT (General Agreement in Trade and Tariff) era. The pharmaceutical industry currently is focused on the identification and development of novel leads from areas such as biotechnology, combinatorial chemistry, molecular modeling, and genetic engineering. The leads coming from these varied sources will require specialized formulation techniques and ingredients. At the same time, the process of discovering new drugs is a costly proposition and requires input from the basic as well as applied sciences. Research organizations that do not have adequate expertise or vision tend to fall out rapidly. The alternative approach for such organizations would be to develop new dosage forms or formulations using novel excipients for the existing drugs that offer distinct benefits over the conventional formulations. Recent developments in pharmaceutical legislation, regulatory guidelines, and licensing policies have led to increased awareness of the properties and roles of excipients in formulations. A careful use of excipients can lead to the development

of novel delivery systems that are both effective and economical. These innovative formulations also may offer life extension to drugs in the form of new patents, extending the product life cycle and adding to the market share of the company.

A formulation can be regarded as a system comprising an active molecule along with some inert ingredients (see Figure 1). According to the definition given by the International Pharmaceutical Excipients Council (IPEC), “Excipients are substances, other than the active drug substance or finished dosage form, which have been appropriately evaluated for safety and are included in drug delivery systems for specific functions” (1). This definition indicates that excipients are to render easy processing of the drug delivery systems, to protect, support, or enhance stability, bioavailability, and patient compliance. They also assist in product identification and are important for overall safety and effectiveness of the drug delivery system during storage or use. These ingredients render specific properties to a formulation and thus represent an important aspect of formulation design and optimization. Selection of the type and amount of excipient is dictated by the target formulation profile and is a major challenge for the pharmaceutical scientist.

Traditionally the ingredients of a formulation “other than active ingredient” were known as inactive ingredients. In the present day, where these inactive ingredients are known to play a crucial role in designing a formulation and to provide desirable characteristics, the term *excipient* is more commonly used. The equivalent of *activity* in an excipient is *functionality*, which refers to special attributes that the ingredient can provide to a formulation. Developing a new excipient is as complicated as developing a new drug molecule; therefore, excipients manufacturers tend to opt for an easier route for value-added specialty excipients. Knowledge and understanding of the ingredients are extremely useful to a product development scientist.

Excipient selection

The choice of an excipient for a particular formulation is governed by various critical parameters spanning from their origin to their regulatory status. These include

- origin, source, and availability
- functional category
- quality and purity
- impurity levels and extent of characterization
- batch-to-batch consistency
- stability in the pure form and in the formulation
- compatibility with the active ingredient and packaging material
- history of prior human use
- safety and toxicological issues
- cost considerations
- biological activity(ies), if any
- regulatory and compendial status
- patent status.

Excipients in vaginal formulations. The vagina has been explored as a favourable site for the local and systemic delivery of drugs used for the treatment of female-specific conditions. Vaginal administration of drugs is mainly used for the treatment of local infections such as vaginitis, bacterial vaginosis, candidiasis, and

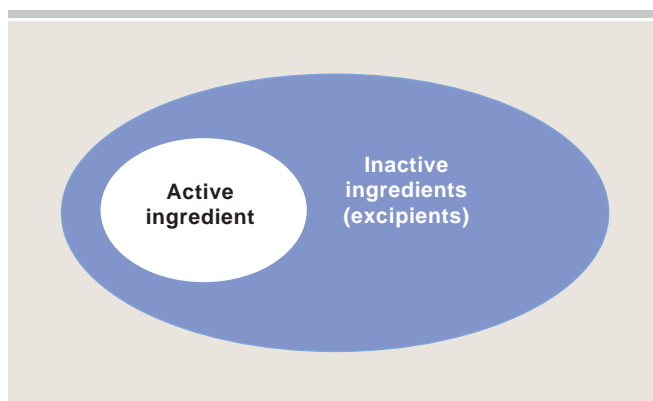


Figure 1: Concept of a formulation.

other infections. In addition, vaginal formulations have a great potential for the systemic absorption of drugs because of the large surface area, rich blood supply, and permeability to a wide range of compounds, including peptides and proteins (2). Vaginally administered agents and formulations are mainly used and are being developed to provide protection against microbial infections, including Acquired Immune Deficiency Syndrome (AIDS) and other sexually transmitted diseases. Known as microbicides, these agents and formulations are also potential vaginal contraceptives.

Several types of formulations are available for intravaginal therapy. These include tablets, hard and soft gelatin capsules, creams, suppositories, pessaries, foams, ointments, gels, films, tampons, vaginal rings, and douches. Figure 2 lists various vaginal dosage forms and the classes of excipients used in them. Vaginal formulations are not only available in modern allopathic systems of medicine but also in traditional systems of medicine such as Ayurveda. Depending on the characteristics of the dosage form, excipients with different functionalities are used.

All excipients present in a vaginal formulation may not be inert and therefore exhibit specific activities, which may affect the primary activity of the active molecule. Recent studies have shown that some excipients possess activities against sexually transmitted pathogens. The ingredients normally used as excipients and possessing potent antimicrobial activities include benzalkonium chloride (3), sodium dodecyl sulfate/sodium lauryl sulfate (4,5), carrageenan (6,7), cellulose acetate phthalate (CAP) (8,9), and undecylenic acid (10). At the same time, several agents being developed as active ingredients have the potential of being used as specialty excipients based on their physicochemical characteristics. Examples of such ingredients include cellulose sulfate (11) and polystyrene sulfonate (12,13).

Methodology

Selecting appropriate excipients for vaginal formulations is a challenge to development scientists. This article is an effort to create a compendium of excipients used (marketed), approved, or investigated for vaginal application. The excipients used in vaginal formulations are relatively less defined in the literature and in regulatory publications in terms of their specific functionalities and toxicities. Information has been compiled from the *FDA Inactive Ingredient Guide* (14), *Handbook of Pharmaceutical Excipients* (15), *Physicians Desk Reference (PDR)*, the Internet, patents, Medline (16), International Pharmaceutical

Table I: Details of excipients present in various vaginal formulations.

Product	Dosage Form	Manufactured or Developed by	Composition	Indication or Therapeutic Use
Aci-Jel	Jelly	Ortho-McNeil Pharmaceutical	Glacial acetic acid, oxyquinoline sulfate, ricinoleic acid, glycerin, tragacanth, acacia, propyl paraben, potassium hydroxide, stannous chloride, egg albumin, potassium bitartrate, perfume, water	Restoration and maintenance of vaginal acidity
Advantage S	Bioadhesive gel	Columbia Laboratories	Water, glycerin, mineral oil, Polycarbophil, hydrogenated palm oil glyceride, Carbomer 934P, methyl paraben, sorbic acid, NaOH	Spermicidal contraceptive
Amino-cerv	Cream	Milex	Urea, sodium propionate, methionine, cystine, inositol	Cervicitis
AVC	Cream, suppository	Monarch	Cream: lactose, propylene glycol, stearic acid, diglycol stearate, methyl paraben, propyl paraben, trolamine, lactic acid Suppository: polyethylene glycol 400 and 3350, Polysorbate 80, glycerin, lactic acid, cover made up of gelatin, glycerin, water, methyl paraben, propyl paraben, color	Vulvovaginitis caused by <i>C. albicans</i>
Betadine	Douche	Purdue Fredrick	—	Vaginal irritation
Buffer gel**	Gel	Reprotect	Carbopol 974P	Maintain vaginal acidity
Savvy/C 31G	Gel	Biosyn	C 31G (as a 10% concentrate), type A gelatin, purified corn starch, hydroxypropylmethyl cellulose, glycerine, water	Microbicide
C 31G*	Suppository	Biosyn	C 31G (as a 10% concentrate), polyethylene glycol 400, 1450, 3350, 8000	Microbicide
Canesten	Cream	Bayer Corp.	Benzyl alcohol, cetyl stearyl alcohol, 1-oatyl dodecanol, Polysorbate 60, water, sorbitan monostearate, spermaceti	Fungal infection, trichomoniasis
Canesten	Insert (tablet)	Bayer Corp.	Adipic acid, colloidal silicon dioxide, lactose, magnesium stearate, maize starch, Polysorbate 80, sodium bicarbonate, stearic acid	Fungal infection, trichomoniasis
Cervidil	Insert	Forest Laboratories	—	Cervical ripening
Cleocin Vag-cream	Cream	Pharmacia & Upjohn	Benzyl alcohol, cetostearyl alcohol, cetyl palmitate, mineral oil, Polysorbate 60, propylene glycol, sorbitan monostearate, stearic acid	Bacterial vaginosis
Clotrimazole	Cream	—	Sodium phosphate, monobasic, adipic acid, colloidal silicon dioxide, lactose, magnesium stearate, maize starch, Polysorbate 80, sodium bicarbonate stearic acid	Yeast infections
Conceptrol	Gel	Ortho-McNeil	Cellulose gum, lactic acid, methyl paraben, povidone, propylene glycol, water, sorbic acid, sorbitol solution	Spermicide, anti-microbial, antiviral
Cortisone-10 Plus	Cream	—	Aloe barbadensis gel, aluminium sulfate, calcium acetate, cetearyl alcohol, cetyl alcohol, corn oil, glycerine, isopropyl palmitate, light mineral oil, maltodextrin, methyl paraben, potato dextrin, propylene glycol, propyl paraben, water, sodium cetearyl sulfate, sodium lauryl sulfate, vitamin A palmitate, Vitamin D and E, white petrolatum, white wax	—
Cortisone-10 Plus	Ointment	—	White petrolatum, benzyl alcohol, propylene glycol, water, SD alcohol	—
Crinone	Gel	Wyeth-Ayerst	Glycerine, mineral oil, Polycarbophil, Carbomer 934P, hydrogenated palm oil glyceride, sorbic acid, sodium hydroxide	Progesterone supplement, ART
Delfen foam	Foam	Ortho-McNeil	Benzoic acid, cellulose gum, cetyl alcohol, glacial acetic acid, methyl paraben, perfume, phosphoric acid, poly vinyl alcohol, propellant A 31, propylene glycol, water, sorbic acid, searamidoethyl diethylamine, stearic acid	Contraceptive
Ecostat	Cream	Bristol-Myers Squibb	Benzoic acid, butylated hydroxy anisole, mineral oil, fragrance, palm oil, polyethylene glycol, Peg stearate	Vaginal infections
Ecostat	Ovule	Bristol-Myers Squibb	Hydrogenated vegetable oil	Yeast infection
Encare	Suppository	Thompson Medical	Polyethylene glycols, sodium bicarbonate, sodium citrate, tartaric acid	Contraceptive
Estrace	Cream	Bristol-Myers Squibb	Propylene glycol, stearyl alcohol, white ceresin wax, glyceryl monostearate, hydroxypropylmethyl cellulose	Vulvovaginal atrophy
Estring	Vaginal ring	Pharmacia & Upjohn	Silicone polymers, barium sulfate	Postmenopausal urogenital atrophy
Femstat	Cream	Bayer Corp.	Cetyl alcohol, glyceryl stearate, polyethylene glycol 100 stearate, methyl paraben, propyl paraben, mineral oil, Polysorbate 60, propylene glycol, sorbitan monostearate, stearyl alcohol, water	Yeast infections
Gynechure	Ointment	Pfizer (Canada)	Aluminium magnesium silicate, butylated hydroxy anisole, white soft paraffin	Vulvovaginal candidiasis
Gynechure	Ovule	Pfizer (Canada)	Bees' wax, gelatin, glycerine, glycine, hydrogenated vegetable fat, lecithin, liquid paraffin, Polysorbate, potassium sorbate, titanium dioxide, water	Vulvovaginal candidiasis
Gyne-Lotrimin	Insert	Schering-Plough	Insert: corn starch, crospovidone, lactose, magnesium stearate, povidone; cream: benzyl alcohol, cetearyl alcohol, cetyl esters wax, octyldodecanol, Polysorbate 60, sorbitan monostearate	Candidiasis
Gyne-Lotrimin	Cream	Schering-Plough	Benzyl alcohol, cetearyl alcohol, cetyl esters wax, octyldodecanol, Polysorbate 60, water, sorbitan monostearate	Candidiasis

Table I, continued.

Product	Dosage Form	Manufactured or Developed by	Composition	Indication or Therapeutic Use
Gynol II	Jelly	Ortho-McNeil	Lactic acid, methyl paraben, povidone, propylene glycol, water, sodium carboxymethyl cellulose, sorbic acid, sorbitol solution	Contraceptive
Intimate Moisture	—	—	Water, polyglyceryl methacrylate, glycerine, sorbitol, propylene glycol, panthenol, sodium hyaluronate, sodium PCA, polyethylene glycol 90M, Carbomer, triethanolamine, diazolidinyl urea, disodium edetate	Vaginal lubricant and moisturizer
Koromex clear	Gel	Quality Health Prod.	—	Contraceptive
Koromex jelly	Jelly	Quality Health Prod.	Boric acid, cellulose gum, fragrance, propylene glycol	Contraceptive
KY Plus	Jelly	Johnson & Johnson	Cremophor, hydroxyethyl cellulose, methyl paraben, propylene glycol, water, sorbic acid	Vaginal moisturizer
Massengill	Douche	SmithKline Beecham	Sodium citrate, citric acid, vinegar, O-9, diazolidinyl urea, cetylpyridinium chloride, EDTA, SD alcohol 40, water	Cleansing aid
Massengill	Towel	SmithKline Beecham	Lactic acid, water, sodium lactate, potassium sorbate, O-9, EDTA, cetylpyridinium chloride, fragrance	Cleanse external vaginal area
Metrogel	Gel	3M Pharmaceuticals	Carbomer 934P, EDTA, methyl paraben, propyl paraben, propylene glycol, sodium hydroxide	Bacterial vaginosis
Monistat	Cream	Ortho McNeil Pharmaceuticals	Benzoic acid, butylated hydroxy anisole, mineral oil, water, Peglicol 5 oleate, Pegoxol stearate	Yeast infection
Monistat	Ovule	McNeil Consumer Products	Gelatin, glycerine, mineral oil, sodium ethyl paraben, titanium dioxide, white petrolatum	Yeast infection
Mycelex 3	Cream	Bayer Consumer Care	Cetyl alcohol, glyceryl stearate, polyethylene glycol 400 stearate, methyl paraben, propyl paraben, mineral oil, Polysorbate 60, propylene glycol, sorbitan monostearate, stearyl alcohol, water	Yeast infection
Mycelex 7	Insert	Bayer Consumer Care	Corn starch, lactose, magnesium stearate, povidone	Yeast infection
Mycelex 7	Cream	Bayer Consumer Care	Benzyl alcohol, cetostearyl alcohol, cetyl esters wax, octyldodecanol, Polysorbate 60, water, sorbitan monostearate	Yeast infection
Mycelex G	Tablet	Bayer Corp.	Lactose, microcrystalline cellulose, hydroxypropylmethyl cellulose, silicon dioxide, magnesium stearate, corn starch, lactic acid, crospovidone	Yeast infection
Myclo-gyne	Cream	Boehringer Ingelheim	Cetyl stearyl alcohol, benzyl alcohol, Polysorbate 60, water, sorbitan monostearate, spermaceti, 2-octyldodecanol	Yeast infection
Myclo-gyne	Insert	Boehringer Ingelheim	Adipic acid, colloidal silicon dioxide, lactose, magnesium stearate, maize starch, Polysorbate 80, sodium bicarbonate, stearic acid	Yeast infection
Ortho-Dienstrol	Cream	Ortho-McNeil	Glyceryl monostearate, peanut oil, glycerin, benzoic acid, glutamic acid, butylated hydroxy anisole, citric acid, sodium hydroxide, water	Atrophic vaginitis, Kraurosis vulvae
Plan B	Tablet	Women's Capital	Colloidal silicon dioxide, potato starch, gelatin, magnesium stearate, talc, corn starch, lactose	Emergency contraceptive
Premarin	Cream	Wyeth-Ayerst Laboratories	Cetyl esters wax, cetyl alcohol, white wax, glyceryl monostearate, propylene glycol monostearate, methyl stearate benzyl alcohol, SLS, glycerin, mineral oil	Atrophic vaginitis
Prepidil	Gel	Pharmacia & Upjohn	Colloidal silicon dioxide, triacetin	Ripening of unfavorable cervix
Prostin E2	Suppository	Pharmacia & Upjohn	Glycerides of fatty acids	Pregnancy termination, Bening hydatidiform mole
Protectaid	Sponge	Axcan Pharma	Polyurethane sponge impregnated with F-5 gel (sodium cholate, benzalkonium chloride, and N-9), polydimethyl siloxane	Contraceptive
Replens	Gel	Columbia Laboratories	Glycerin, mineral oil, Polycarbophil, hydrogenated palm oil glyceride, Carbomer 934 P, methyl paraben, sorbic acid, sodium hydroxide, water	Vaginal moisturizer
Semiced	Insert	Whitehall Robins	Benzethonium chloride, citric acid, methyl paraben, water, PEG	Spermicidal
Sultrin	Cream	Ortho-McNeil Pharmaceutical	Cetyl alcohol, cholesterol, diethylaminoethyl stearamide, glyceryl monostearate, lanolin, lecithin, methyl paraben, peanut oil, phosphoric acid, propylene glycol, propyl paraben, water, urea, stearic acid	Vaginitis caused by Gardnerella
Terazol	Suppository	Ortho-McNeil	Butylated hydroxy anisole, palm kernel oil, coconut oil, glycerides	Moniliasis
Terazol 3	Cream	Ortho-McNeil	Butylated hydroxy anisole, cetyl alcohol, isopropyl myristate, Polysorbate 60 and 80, propyl glycol, stearyl alcohol, water	Moniliasis
Today	Sponge	Whitehall Robins	Benzoic acid, citric acid, sorbic acid, water, sodium dihydrogen citrate, sodium metabisulfite in a polyurethane sponge	Spermicidal
Vaginal Contraceptive Film	Film	Apothecus Pharmaceutical	Glycerine, poly vinyl alcohol	Spermicidal

* Phase II with chlamydia and gonorrhoea end points in planning stage (19).

** Phase I/II post-coital contraceptive effectiveness trial nearing completion (19).

Table II: Excipients used, approved, or investigated for vaginal formulations.

Excipient	Category (concentration in %)	Regulatory Status
Absorbent cotton	absorbent sutures in tampons	8, 13, 25
Acacia	suspending agent (5–10); emulsifier (5–10); tablet binder (1–5); pastille base (10–30)	I, 3, 8, 25
<i>Adipic acid</i>	acidifier; urethane foams	–
<i>Adonitol</i>	sugar	–
<i>Agarose</i>	gelling agent; thickening agent	–
Alcohol	solvent	1, 3, 5–7, 9–14, 16–19, 21–26
<i>Alkyl fumarate</i>	buffering agent	–
Allantoin	adsorbent; clarifying agent (1–2); emulsion stabilizer (1.0); suspending agent (0.5–5.0)	1, 3, 6–11, 13–14, 16–18, 20, 23, 25
Alum, potassium	astringent; antiseptic	I, 8, 25
Aluminium magnesium silicate (Veegum)	adsorbent (10–50); binder (2–10); disintegrant (2–10); suspending agent (1–10); emulsifier (2–5); thickening agent (2–10)	3, 25
Aluminium sulfate	acidifier; mineral carrier for adsorbed vaccines	13, 25
<i>Arabitol</i>	sugar	–
Ascorbic acid	antioxidant (0.01–0.1)	G, 1, 3v, 3–26
Barium sulfate	diagnostic aid (radiopaque medium)	I, 8, 13, 25
Bentonite	adsorbent (1–2); emulsion stabilizer (1.0); suspending agent (0.5–5.0); viscosity enhancer	I, 1, 3, 6–11, 13–14, 16–18, 20, 23, 25
Benzalkonium chloride	preservative (0.01–0.02)	1, 3, 3v, 4, 7–9, 11–12, 14, 16–18, 20, 23–26
Benzethonium chloride	preservative (0.01–0.02)	7, 16, 19, 25
Benzoic acid	preservative (0.1–0.2)	G, 1–26
Benzyl alcohol	preservative (<2); solubilizer (≥5); disinfectant (10)	1, 3, 7–9, 11–14, 16–20, 23, 25
Beta cyclodextrin	stabilizing agent; solubilizing agent	25
Boric acid	astringent; antimicrobial preservative	3, 8, 25
Butylated hydroxyanisole	antioxidant (0.005–0.02)	G, 3, 9, 13, 14, 17, 25
Butylated hydroxytoluene	antioxidant (0.5–1.0)	G, 3, 8–10, 13, 17–19, 23, 25
Calcium acetate	food stabilizer; buffering agent	3, 8, 25
Calcium carbonate	diluent; buffering and dissolution aid in dispersible tablets; bulking agent in sugar coating	G, 1–4, 6–21, 23–26
Calcium lactate	buffering agent; preservative	I
Carbomer (Carbopol)	emulsifying agent (0.1–0.5); gelling agent (0.5–2.0); suspending agent (0.5–2.0) tablet binder (5–10)	3, 14, 17, 25
Cellulose	diluent (0–100); binder (5–20); disintegrant (5–15); glidant (1–2)	G, 3, 8–11, 14, 18, 20, 23, 25
Ceteth-20 (Polyoxyethylene 20 cetyl ether)	emulsifying agent; wetting agent; solubilizer; antifoaming agent; vaginal tampons	I
Cetostearyl alcohol (Cetearyl alcohol)	stiffening agent; emulsifying agent; gelling agent (10); suppository base	1, 3, 3v, 6, 8, 10, 13, 21, 25, 26
Cetyl alcohol	coating agent; emulsifying agent (2–5); stiffening agent (2–10); emollient (2–5); water absorption base (5)	1, 3, 6, 8–10, 14, 16–19, 23, 25–26
<i>Cetyl dimethicone copolyol</i>	antifoaming agent	–
Cetyl esters wax	cold cream base (12.5); stiffening agent (1–20); emollient	25
Cetyl palmitate	emulsion/cream base; stiffening agent; emollient	I
Cetyl pyridinium chloride	preservative	25
Chamomile tea	soothing agent	–
<i>Chitosan</i>	gelling agent; sustained-release formulations	–
Cholesterol	emulsifying agent (0.3–5.0); emollient	1, 4, 6, 16, 21, 25
Choleth	emulsion/cream base	I
Citric acid	acidifier; sequestering agent (0.3–2.0); effervescent formulations; antioxidant synergist	G, 1, 3–14, 16–26
Cocoa butter (Theobroma oil)	suppository/ointment base	3, 8, 25
Coconut oil glycerides	suppository/ointment base	8
Collagen	absorbent sutures in medicated tampons	8, 25
Colloidal Silicon dioxide	adsorbent; anticaking agent; glidant (0.1–0.5); suspending and thickening agent (2–10); tablet disintegrant; emulsion stabilizer (1–5)	G, 1, 3, 8–14, 16–18, 20, 23, 25
Copper sulfate	astringent, antiseptic	8, 25
Corn oil (maize oil)	solvent	3, 8, 25
Cremophor	emulsifier; solubilizer	25
Crospovidone	tablet disintegrant (2–5)	14, 17, 25
Cystine	wound healing	8
Dextrin	suspending agent; binder; diluent	G, 1, 3, 5, 6, 9, 10, 16, 17, 25, 26
Dextrose	diluent; tonicity adjusting agent; sweetening agent	3v, 1–5, 8–11, 13–4, 17–20, 22–26

Table II, continued

Excipient	Category (concentration in %)	Regulatory Status
Diacetin	plasticizer; softening agent; solvent	–
<i>Diacetyl phosphate</i>	phospholipids for liposomes	–
Dibasic calcium phosphate	diluent	G, 1–3, 8–14, 16–20, 22–23, 25–26
Dichlorodifluoromethane	aerosol propellant	17, 25
Dichlorotetrafluoro-ethane (Cryofluorane)	aerosol propellant	17, 25
Diethylaminoethyl stearamide	cream base	–
Diglycol stearate	emulsifying agent; dispersing agent	I
Disodium edetate	chelating agent	G, 2, 3, 8, 9, 11–14, 16–20, 23–26
<i>Dulcitol (Galactitol)</i>	pharmaceutical aid	–
EDTA	chelating agent; antioxidant synergist (0.005–0.1); preservative synergist (0.01–0.1)	21, 25
Egg albumin	jellying agent	G
Ethyl cellulose	coating agent (1–3); tablet binder (1–3); viscosity enhancer	G, 3, 8, 17, 25
Ethylene glycol	humectant; solvent; cosolvent	I
Fragrance (RBD–9819)	fragrance	I
Gelatin	hard and soft capsules; microencapsulation; base for paste, pastilles, pessaries, and suppositories; viscosity enhancer; tableting aid; coating agent; film former; suspending agent	1, 3–14, 16–26
Glacial acetic acid	acidifier; preservative; solvent	8, 25
Glutamic acid	acidifier	I, 8
Glycerides of fatty acids	suppository base	1, 3–14, 16–26
Glycerin	humectant (<30); preservative (>20); emollient (<30); plasticizer; solvent (<50)	G, 1, 3v, 3–14, 16–21, 23–26
<i>Glycerogelatin</i>	suppository base (2–6)	–
Glyceryl monostearate	emulsifier; stabilizer; emollient; plasticizer; tableting aid	G, 1, 3, 8–10, 12–14, 23, 25, 26
Glyceryl stearate	emulsifying agent; stabilizer; emollient; plasticizer; tablet lubricant; sustained-release tablets	G, 12, 25
Glycine	buffering agent	8, 3, 13, 25
<i>Glycogen</i>	animal starch	–
Guar gum	emulsion stabilizer (1); tablet binder (>10); disintegrant; thickener (>2.5)	G, 9, 13, 25
Hibitane acetate	preservative	3, 5, 8, 10, 15, 18, 23
Hydrochloric acid	acidifier	G, 1–3, 3v, 5, 7–14, 16–25
Hydrogen peroxide	antiseptic; deodorant; cleansing agent	8, 3, 13, 25
Hydrogenated palm oil glyceride	emulsion/cream base	–
Hydrogenated vegetable oil	tablet and capsule diluent; lubricant (1–6); binder	G, 16, 25
Hydrous lanolin	emulsifying agent; ointment base	1, 3, 4, 6, 8–10, 13–14, 16, 18, 19, 21–23, 25
Hydroxyethyl cellulose	thickening agent; gelling agent; binding agent; film former	3, 8, 9, 10–12, 18, 20, 23, 25
<i>Hydroxyethyl methacrylate</i>	viscosity enhancer; hydrogel ingredient	–
Hydroxymethyl cellulose	gelling agent; thickening agent	I
Hydroxypropyl cellulose	coating agent (3–5); film former; emulsifying agent; sustained-release matrix (15–35); thickening agent; suspending agent; stabilizing agent	G, 3, 8–10, 12, 14, 16, 18, 20, 23, 25
Hydroxypropylmethyl cellulose	film former (2–10); tableting aid (2–10); suspending and thickening agent (0.45–1); emulsifier; gelling agent (2–10)	G, 3, 8, 9, 11, 14, 16, 18, 20, 23, 25
Inositol	sugar, supports epithelialization	–
Isopropyl myristate	detergent (0.003–0.03); topical creams and lotions (1–10); emollient; oleaginous vehicle; skin penetrant	1, 3, 8, 13, 25
Isopropyl palmitate	detergent (0.005–0.02); perfume (0.2–0.8); emollient; oleaginous vehicle; solvent	3, 8, 25
Lactic acid	acidifier; topical preparations (0.015–6.6)	G, 1, 3–14, 16–21, 23–26
Lactose	tablet and capsule excipient (65–85); vaginal suppository and emulsion	1–3, 3v, 5–14, 16–26
Lanolin	emulsifying agent; ointment base	3v, 1–14, 16–26
Laureth (Polyoxyethylene lauryl ether)	emulsifier; solubilizing agent; wetting agent	I
Lecithin	emollient; emulsifying agent; solubilizing agent; suppository base	G, 1, 17, 25
Light mineral oil (light paraffin)	emollient; solvent; tablet and capsule lubricant; oleaginous vehicle (<50)	G, 2, 3, 3v, 8–11, 13–14, 16, 18, 20, 23, 25
Magnesium stearate	tablet and capsule lubricant (0.25–5)	G, 1–3, 5, 6, 8–10, 12–14, 16–21, 23, 25, 26
Maltodextrin	film coating (2–10); tablet binder (2–40); viscosity enhancing agent; diluent	G, 25
Maltose (liquid glucose)	coating agent (10–20); binder (5–10); sweetening agent (20–60)	8, 25

Table II, continued

Excipient	Category (concentration in %)	Regulatory Status
Mannitol	sweetening agent; diluent (20–90); thickening agent (<7); plasticizer in soft gelatin capsules; tonicifier	G, 1, 3–9, 11–19, 21, 23, 24, 26
Massa estarinum	suppository base	1, 3, 3v, 8–12, 14, 18–20, 23, 25
Massupol	suppository base	1, 3, 3v, 8–12, 14, 18–20, 23, 25
Methionine	mild acidifier; wound healing	8, 13, 25
Methyl cellulose	emulsifying agent (1–5); suspending agent (1–2); binder (2–6); tablet coating (0.5–5); tablet disintegrant (2–10); sustained-release tablet matrix (5–75); gelling agent	G, 1, 3–4, 6, 8–9, 12, 14, 16, 18, 20–23, 25, 26
Methyl paraben	preservative (0.1–0.18)	G, 1, 3–4, 7–14, 16–21, 23, 25–26
Methyl stearate	cream base	–
Microcrystalline cellulose	disintegrant (5–15); diluent (20–90); adsorbent (20–90); anti-adherent (5–20)	G, 3, 8, 9, 11–14, 16–18, 20, 23, 25
Mineral oil	emollient; solvent (1–32); tablet and capsule lubricant; oleaginous vehicle (0.1–95)	G, 3v, 1–14, 16–26
Myristic acid	cream base; sustained-release preparations	I
N 3 chloroallyl methenamine chloride	antiseptic	I
Nitric acid	acidifier	I, 3
Novata	suppository base	1, 3, 3v, 8–12, 14, 18–20, 23, 25
Octyl dodecanol	vaginal emulsion; cream and suppository	I
Oxyquinoline sulfate	chelating agent; deodorant; antiseptic	25
Palm kernel oil	suppository/ointment base	I, 3
Palm oil	suppository/cream base	I
Panthenol	vitamin	25
Peanut oil	solvent; oleaginous vehicle	1, 3, 3v, 6–11, 13–14, 16–20, 23, 25
Peglicol 5 oleate	water-miscible cream base	I
Pegoxol 7 stearate	water-miscible cream base	I
Phenylethyl alcohol	preservative (0.25–1.0)	19, 25
Phosphoric acid	acidifier; synergistic antioxidant; solvent	8, 13, 25
Piperazine hexahydrate	solubilizer, stabilizer (for estrogen)	I, 8
Poloxyethylene stearates	emulsifying agent (0.5–10); solubilizing agent; wetting agent; tablet lubricant (1–2); ointment base (7)	1, 4, 10, 12, 16, 23, 25
<i>Polyacrylamide</i>	gelling agent (4)	–
Polycarbophil	gelling agent; controlled release; bioadhesive; viscosity modifier; complexing agent; moisture enhancer	25
Polyethylene	suppository base	I
Polyethylene glycol	suppository/ointment base; plasticizer; solvent; tablet and capsule lubricant	1–4, 6–10, 12, 14, 16, 18–21, 23, 25, 26
Polyethylene glycol (Polyoxyl stearate)	emulsifying agent	1, 4, 10, 12, 16, 23–25
Polyethylene oxide	sustained-release formulation	I, 25
Polyglyceryl methacrylate	matrix former	–
Polyoxyethylene – Polyoxypropylene copolymer (Pluronic/ Poloxamer)	gelling agent (15–50); fat emulsifier (0.3); flavor solubilizer (0.3); spreading agent (1); stabilizing agent (1–5); suppository base (4–6 or 90); tableting aid (5–10); wetting agent (0.01–5)	I, 3, 25
Polysorbates	emulsifier (1–15); solubilizing agent (1–10); wetting agent (0.1–3)	G, 1, 3–6, 8–14, 25, 16, 18–21, 23
Polyvinyl alcohol	coating agent; surfactant; viscosity enhancing agent; film former; topical lotions (2.5)	12, 17, 25, 26
Potassium bitartrate	acidifier	–
Potassium carbonate	alkalinizer; effervescent formulations	I
Potassium hydroxide	alkalinizer	I, 8
Potassium sorbate	preservative (0.1–0.2)	G, 3, 9, 14, 18, 23, 25
Povidone (Polyvinyl pyrrolidone)	suspending agent (<5); tablet binder; diluent; coating agent (0.5–5)	G, 3, 9, 14, 18, 23, 25
Pregelatinized starch	diluent (5–75); tablet binder (5–20); tablet disintegrant (5–10)	3, 25
Promulgen D	emulsion/cream base	I
propellant A31	propellant	–
Propyl paraben	preservative (0.02–0.1)	G, 1, 3–4, 6–11, 13–14, 16–21, 23, 25, 26
Propylene glycol	humectant (15); preservative (15–30); solvent or cosolvent (5–80)	G, 1, 3, 3v, 4, 6–14, 16–20, 23–26
Propylene glycol monostearate	emulsion base	
Quillaia saponins	emulsifier	3
Rayon	absorbent sutures in tampons, surgical aid	25
Ricinoleic acid	used in contraceptive jellies	–

Table II, continued

Excipient	Category (concentration in %)	Regulatory Status
<i>Salvaderm pink perfume</i>	perfume	—
SD Alcohol 40	solvent	—
Silica gel	disintegrant in vaginal capsules (2–5); tableting aid	I
Silicone polymers (Polydimethylsiloxane/ Dimethicone/ Simethicone)	oleaginous ointment base; antifoaming agent; lubricant, wetting agent; adhesives; surfactant; vaginal rings	I, 3, 8, 13, 25
Sodium alginate	stabilizer (1–3); suspending agent (1–5); disintegrant (2.5–10); binder (1–3); viscosity enhancer (5–10)	G, 1, 3, 8–10, 14, 17, 18, 23, 25
Sodium ascorbate	antioxidant	G, 9, 13, 25
Sodium benzoate	preservative (0.02–0.5); tableting aid (2–5)	G, 1–9, 11–14, 16–26
Sodium bicarbonate	alkalinizer (10–40); effervescent preparations (25–50)	G, 3v, 1–26
Sodium carbonate	buffering agent; effervescent preparations	I, 8, 25
Sodium carboxymethyl cellulose	emulsifying agent (0.25–1.0); gelling agent (4–6); tablet binder (1–6)	G, 1, 3, 4, 6–9, 11–14, 16–19, 21, 23, 25, 26
Sodium chloride	humectant, tableting aid (5–80), capsule diluent (10–80); flocculating agent for suspensions (<1), isotonic solutions (<0.9)	G, 3v, 1–26
Sodium cetearyl sulfate (sodium cetostearyl sulfate)	surfactant	8
Sodium citrate	buffering agent (0.3–2); sequestering agent (0.3–2)	G, 1, 3, 3v, 5–26
Sodium dibasic phosphate	buffering agent; sequestering agent	G, 1–3, 6–14, 16–21, 23, 25, 26
Sodium dihydrogen citrate	buffering agent	—
Sodium ethyl paraben	preservative	3, 5, 9, 16, 25
Sodium hyaluronate	viscosity enhancing agent	—
Sodium hydroxide	alkalinizer	I, 8, 13, 25
Sodium lactate	alkalinizer	I, 8, 13, 25
Sodium lauryl sulfate	anionic emulsifiers (0.5–2.5); solubilizer (at critical micelle concentration >0.25); tablet lubricant (1–2); wetting agent (1–2)	G, 1–4, 6–9, 11–13, 16, 18, 21, 23, 25, 26
Sodium metabisulfite	antioxidants (0.01–1)	G, 1–3, 3v, 6–9, 12, 13, 16–19, 24–26
Sodium monobasic phosphate	alkalinizer; sequestering agent; emulsifying agent	G, 3v, 1–5, 8–14, 17–20, 23, 25, 26
Sodium propionate	preservative (5–10)	G, 3v, 9, 19, 25
Sodium propyl paraben	preservative	3, 9, 13, 14, 25
Sodium starch glycolate	tablet and capsule disintegrant	3, 13, 14, 17, 25
Sorbic acid	preservative (0.05–0.2)	G, 1–3, 6, 8–10, 12, 14, 17–18, 23, 25–26
Sorbitan esters (stearates, laurates, oleates, and palmitates)	emulsifier (1–50); solubilizer (1–10); wetting agent (0.1–3)	3, 12, 16, 17, 23, 25, 26
Sorbitol	humectant (3–15); plasticizer (5–20); vehicle in sugar-free liquid formulations (20–70); tableting aid (25–90)	G, 1, 3, 6–14, 16–18, 20, 21, 23, 25, 26
Spermaceti wax	ointment/emulsion base; emollient; stiffening agent	I
Stannous chloride	reducing agent	I, 8
Starch (potato, maize)	glidant; diluent; disintegrant (3–15); tablet binder (5–25)	G, 3v, 1–14, 16–21, 23–26
Stearic acid	tableting aid (1–3) ointment and cream base (1–20) emulsifying and solubilizing agent	G, 1–7, 9, 12–14, 16–17, 19, 21, 23, 25–26
Stearyl alcohol	stiffening agent; emollient; weak emulsifying agent; tableting aid	3, 8, 9, 14, 16, 17, 25
Succinic acid	acidifier	I
Sucrose	tablet binder (2–67); suspending agent; viscosity enhancer	G, 1–3, 5–14, 16–21, 23–26
Suppocire	suppository base	1, 3, 3v, 8–12, 14, 18–20, 23, 25,
<i>Synthetic fiber composed of polyester, polypropylene, nylon, or acrylic resin</i>	base material for tampons	—
Talc	dusting powder (90–99); glidant and tablet lubricant (1–10); diluent (5–30)	G, 1, 3, 3v, 5–14, 16, 18–22, 24–26
Tartaric acid	acidifier; sequestering agent; antioxidant synergist; effervescent formulations	G, 1, 3–4, 6–14, 16–21, 23–26
Tartrazine (FD&C yellow #5)	coloring agent	I
<i>Tertiary butyl hydroquinone</i>	antioxidant (<0.02)	—
Titanium dioxide	coating agent; pigment	1–4, 8–9, 11–14, 16–18, 20, 23, 25, 26
Tragacanth	suspending agent; viscosity modifier	G
Triacetin	plasticizer (10–35)	G, 8, 25
Triethanolamine (Trolamine)	alkalinizer; emulsifying agent (2–4); humectant; solvent; polymer plasticizer	1, 3–4, 6–7, 9, 12, 14, 16–19, 23, 25–26
Trihydroxystearate	cream base	I
Urea	antiseptic	I, 3, 8, 13, 25

Table II, continued

Excipient	Category (concentration in %)	Regulatory Status
Vitamins A, D, and E	vitamins	1, 3, 13, 25
Water	solvent	1–3, 3v, 5–14, 16–21, 23–26
White ceresin wax (white microcrystalline wax)	stiffening agent; tablet and capsule coating agent	G, 23, 25
White soft paraffin (Petrolatum)	absorption base component (10–50); emollient; plasticizer (5–50)	1, 3v, 3–5, 7, 9–10, 12–14, 16–21, 23–26
White wax (bleached bees' wax)	stiffening agent (5–20); emulsifying agent; polishing agent for sugar coating; sustained-release formulations; helps in adjusting melting point of suppositories	G, 1–3, 3v, 6–14, 16–21, 23, 25–26
Witepsol (Wecobee)	suppository base	1, 3, 3v, 8–12, 14, 18–20, 23, 25,
Xanthan gum	bioadhesive; stabilizing agent; suspending agent; viscosity enhancer	G, 1, 8, 17, 25
Xylitol	sweetening agent; pharmaceutical aid	G, 6, 8, 16, 25

Abbreviations: G: GRAS, I: inactive ingredients guide, Pharmacopeias, 1: Austrian, 2: Belgian, 3: British, 3v: British (veterinary), 4: Brazilian, 5: Chinese, 6: former Czechoslovakian, 7: Egyptian, 8: European, 9: French, 10: German, 11: Greek, 12: Hungarian, 13: Indian, 14: Italian, 15: International, 16: Japanese, 17: Mexican, 18: Netherlands, 19: Nordic, 20: Portuguese, 21: Romanian, 22: Russian, 23: Swiss, 24: Turkish, 25: United States, 26: former Yugoslavian

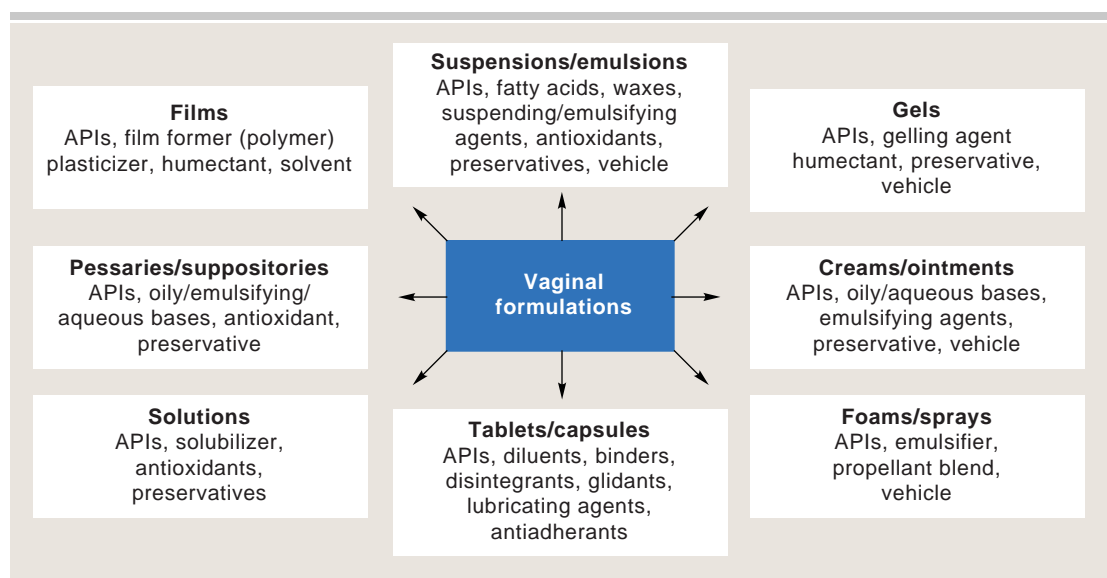


Figure 2: Vaginal formulations and the classes of excipients added to these formulations. API = active pharmaceutical ingredient.

marketed were studied from sources such as patents, Medline search, and research publications. Once a list of marketed or investigated excipients was compiled, further information about each of those ingredients such as their functional categories, concentration used (not necessarily for vaginal application, but for human use), and regulatory status was collected from sources such as *Handbook of Phar-*

maceutical Excipients, FDA's inactive ingredients guide, pharmacopeias, etc. (see Table II). Some excipients in vaginal formulations have been investigated or patented but never marketed or even approved for human application. These are listed in italics in Table II. One needs to be extremely careful while selecting such excipients because these will require detailed toxicological studies before approval for inclusion in a formulation to be marketed. Also, the list is not exhaustive because of reasons explained and does not offer any kind of regulatory authority to the end users.

Abstracts (IPA), official compendia, the *Federal Register*, standard textbooks, and databases of formulation science from allopathic and alternative systems of medicine, relevant publications such as abstracts from Microbicide 2000 and the Preclinical Evaluation Workshops, and other sources. The information provided in this article can serve as a ready reference for selection of appropriate excipients during the development of vaginal formulations. Thus, formulation development scientists entrusted with the task of developing novel vaginal formulations will find this article of great use during their development work.

The following protocol was followed to collect and present the compendium. In the first phase, information about excipients from marketed vaginal products was collected from various sources and compiled as Table I. There is no way to find inactive ingredients used in marketed formulations in several countries such as India because it is not a legal requirement to list them on the label, and the information is usually kept proprietary.

In the next step, excipients investigated but not necessarily

marketed were studied from sources such as patents, Medline search, and research publications. Once a list of marketed or investigated excipients was compiled, further information about each of those ingredients such as their functional categories, concentration used (not necessarily for vaginal application, but for human use), and regulatory status was collected from sources such as *Handbook of Phar-*

maceutical Excipients, FDA's inactive ingredients guide, pharmacopeias, etc. (see Table II). Some excipients in vaginal formulations have been investigated or patented but never marketed or even approved for human application. These are listed in italics in Table II. One needs to be extremely careful while selecting such excipients because these will require detailed toxicological studies before approval for inclusion in a formulation to be marketed. Also, the list is not exhaustive because of reasons explained and does not offer any kind of regulatory authority to the end users.

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