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[54] **TOPICAL FORMULATIONS FOR THE TREATMENT OF NAIL FUNGAL DISEASES**

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[52] **U.S. Cl.** **514/655**

[58] **Field of Search** 514/655

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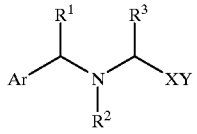
[57] **ABSTRACT**

Stable, topical formulations useful for treating a nail fungal disease are disclosed. The compositions comprise an antifungal compound and at least one pharmaceutically acceptable excipient sufficient to form a gel. The antifungal compound is represented by the formula



where R^1, R^2, and R^3 are independently hydrogen or lower alkyl; X is $—(CH_2)_n—$ in which n is 0, 1 or 2; Y is aryl or heteroaryl; and Ar is aryl or heteroaryl. The composition is applied to the afflicted nail for once a day until the fungal disease is cured.

22 Claims, No Drawings

TOPICAL FORMULATIONS FOR THE TREATMENT OF NAIL FUNGAL DISEASES

This application claims the benefit of U.S. Provisional Application No. 60/082187, filed Apr. 17, 1998.

TECHNICAL FIELD

The invention relates to stable topical formulations useful for the treatment of nail fungal diseases and a method of treating fungal diseases in nails.

BACKGROUND

Many methods are known for the treatment of fungal infections, including the oral and topical use of antibiotics (e.g. nystatin and amphotericin B), imidazole antifungal agents such as miconazole, clotrimazole, fluconazole, econazole and sulconazole, and non-imidazole fungal agents such as the allylamine derivatives terbinafine and naftifine, and the benzylamine butenafine.

Onychomycosis is a fungal infection of the nail unit caused by yeast, dermatophytes, or other molds, and represents approximately 50% of all nail disorders. Toenail infection accounts for approximately 80% of onychomycosis incidence, while fingernails are affected in about 20% of the cases. Dermatophytes are the most frequent cause of nail plate invasion, particularly in toenail onychomycosis. Onychomycosis caused by a dermatophyte is termed tinea unguium. *Trichophyton rubrum* is by far the most frequently isolated dermatophyte, followed by *T. mentagrophytes*. Distal subungual onychomycosis is the most common presentation of tinea unguium, with the main site of entry through the hyponychium, progressing in time to involve the nail bed and the nail plate. The disease is characterized by discoloration, onycholysis, accumulation of subungual debris and nail plate dystrophy. Diagnosis can be confirmed by KOH (potassium hydroxide) preparations and mycologic culture. The disease adversely affects the quality of life of its victims, with subject complaints ranging from unsightly nails and discomfort with footwear, to more serious complications including secondary bacterial infections.

Onychomycosis has proved to be resistant to treatment. Nail fungal infections reside in an area difficult to access by conventional topical treatment, and antifungal drugs cannot readily penetrate the nail plate to reach the infection sites under the nail. Therefore, onychomycosis has traditionally been treated by oral administration of antifungal drugs; however, clearly this is undesirable due to the potential for side effects of such drugs, in particular those caused by the more potent antifungal drugs such as itraconazole and ketoconazole. An alternative method of treatment of onychomycosis is by removal of the nail before treating with a topically active antifungal agent; such a method of treatment is equally undesirable.

Onychomycoses do not resolve spontaneously, and even if successfully treated, tend to recur. Treatment of onychomycosis is often a challenging endeavor for the clinician. Systemic antimycotic agents require prolonged use and have the potential for significant side effects. Topical agents have usually been of little benefit.

It would therefore be advantageous to have a topical formulation that is capable of penetrating the nail barrier and effectively treating nail fungal diseases, thus avoiding oral administration of antifungal drugs and the necessity of removing the nail. It would be preferable if such treatment required only nightly applications of the formulation, i.e. effective treatment did not require that the formulation be

resident 24 hours per day on the nails over a long period of time. This patent application describes such a formulation.

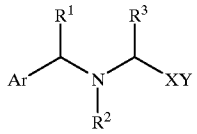
Publications of interest are WO 96/19186, U.S. Pat. No. 4,746,509, U.S. Pat. No. 4,822,822, U.S. Pat. No. 5,322,685, PCT Application US92/10989, EP Patent Application 55,397, GbB2, 202, 743A; and CA 1,175,355.

SUMMARY OF THE INVENTION

The present invention relates to a composition and a method for treating a fungal disease in a nail of a mammal, particularly a human. In particular, the invention relates to a stable topical formulation useful for the treatment of a nail fungal disease, comprising an antifungal agent and one or more pharmaceutically acceptable excipients sufficient to form a gel capable of delivering the antifungal through the nail barrier.

One aspect of the invention relates to a topical antifungal composition that comprises

(a) an antifungal compound of the formula:



wherein:

R^1, R^2, and R^3 are independently hydrogen or lower alkyl;

X is $—(CH_2)_n—$, in which n is 0, 1 or 2;

Y is aryl or heteroaryl; and

Ar is aryl or heteroaryl, or a pharmaceutically acceptable salt thereof, in combination with

(b) one or more pharmaceutical excipients sufficient to form a composition capable of adhering to the surface of the nail to deliver the antifungal through the nail barrier.

Another aspect of the invention is a method of treating a nail fungal disease by application to the nail of a mammal the claimed topical composition. The process comprises

(a) applying a therapeutically-effective amount of the antifungal composition to the surface of the nail to be treated,

(b) maintaining the composition on the nail for up to about 24 hours (preferably about 4 to about 12 hours),

(c) removing the composition for a short time, preferably for about 4 to about 12 hours, and

(d) repeating steps (a) through (c) until the fungal disease has been successfully treated.

Yet another aspect of the invention pertains to the use of the antifungal compound for the preparation of a topical composition for the treatment of a nail fungal disease, wherein a therapeutically-effective amount of the topical composition is (a) applied to the surface of the nail to be treated, (b) maintained on the nail for up to about 24 hours (preferably about 4 to about 12 hours), (c) removed for a short time, preferably for about 4 to about 12 hours, and (d) steps (a) through (c) are repeated until the fungal disease has been successfully treated.

Another aspect of the invention is an article of manufacture comprising the claimed topical composition in a container in combination with labeling instructions for application of the topical compositions in the treatment of nail fungal diseases.

Another aspect of the invention is an article of manufacture comprising the composition in combination with a covering device to retain the composition on the nail

DETAILED DESCRIPTION AND PRESENTLY PREFERRED EMBODIMENTS

This invention is useful for topically treating onychomycosis, i.e. a flngal infection of the nail plate on the hands or feet of mammals, particularly humans. The nail fungal disease is usually caused by Epidermophyton, Microsporum, and/or Trichophyton and produces nails that are opaque, white, thickened, friable and brittle. Onychomycosis is sometimes called ringworm of the nails or tinea unguis. The composition delivers an antifungal compound to the nail plate (the stratum corneum unguis) and to the nail bed (the modified area of the epidermis beneath the nail, over which the nail plate slides as it grows) through the nail plate and around the nail periphery. Desirably the antifungal compound is also concurrently delivered to the nail matrix, the cuticle and the hyponychium (the thickened epidermis underneath the free distal end of a nail).

The invention has several aspects. One aspect is the composition itself. Another aspect is the use of the composition to treat onychomycosis. Still another aspect is, an article of manufacture, i.e., the composition in combination with printed labeling instructions explaining how to use the composition for the desired results. Still another aspect is an article of manufacture that comprises the combination of the composition with a covering adapted to retain the composition on the nail for an extended period of time.

Definitions

As used herein:

"Alkyl" means a branched or unbranched saturated monovalent hydrocarbon radical containing 1 to 12 carbon atoms, such as methyl, ethyl, propyl, isopropyl, tert-butyl, butyl, n-hexyl, dodecyl, and the like, unless otherwise indicated.

"Lower alkyl" means a branched or unbranched saturated monovalent hydrocarbon radical containing 1 to 6 carbon atoms, such as methyl, ethyl, propyl, isopropyl, tert-butyl, butyl, n-hexyl and the like, unless otherwise indicated.

"Lower alkoxy" means the group —O—(lower alkyl) wherein lower alkyl is as herein defined.

"Lower alkyl ethers of propylene glycol" refers to compounds of the formula (lower alkyl)—O—CH_2—CH_2(CH_3)—O—(lower alkyl).

"Lower fatty acid esters of propylene glycol" refers to compounds of the formula (lower alkyl)—C(O)O—CH_2—CH_2(CH_3)—OC(O)—(lower alkyl).

"Alkylene" means a branched or unbranched saturated divalent hydrocarbon radical containing 1 to 12 carbon atoms, such as methylene, ethylene, 1,2-propylene, 1,4-butylene, 1,3-butylene, 1,5-pentylene, 1,3-pentylene, 1,6-hexylene, 1,12-dodecylene, and the like.

"Alkenylene" means a branched or unbranched unsaturated divalent hydrocarbon radical containing 2 to 12 carbon atoms, such as ethene, 1-propene, 1-butene, 3-methylbut-1-ene, 1-pentene, 2-methylpent-1-ene, 1-hexene, 1-dodecene, and the like.

"Halo" means fluoro, chloro, bromo, or iodo.

The term "aryl" refers to a monovalent unsaturated aromatic carbocyclic radical having a single ring (e.g., phenyl) or two rings (e.g., naphthyl, biphenyl, indanyl, 1,2,3,4-tetrahydronaphthyl, benzocycloheptane), which can optionally be mono-, di- or tri-substituted, independently, with OH, COOH, lower alkyl, lower alkoxy, halo, nitro, amino, alkylamino, dialkylamino, trifluoromethyl and/or cyano.

The term "heteroaryl" refers to a monovalent aromatic carbocyclic radical having 1–3 heteroatoms within one or two rings, (e.g., thiophenyl, fuiranyl, pyridyl, thiazolyl, pyrimidine, oxazolyl, benzoxazole, benzofuran, benzothiophene, indolinyl, quinoline), which can optionally be mono-, di- or tri-substituted, independently, with OH, COOH, lower alkyl, lower alkoxy, halo, nitro, amino, alkylamino, dialkylamino, trifluoromethyl and/or cyano.

The term "heteroatom" refers to oxygen, sulfur or nitrogen, unless otherwise specified.

"Optional" or "optionally" means that the subsequently described event or circumstance may or may not occur, and that the description includes instances where said event or circumstance occurs and instances in which it does not. For example, "optionally substituted phenyl" or "optionally substituted naphthyl" means that the phenyl or naphthyl may or may not be mono-, di- or tri-substituted, independently, with OH, COOH, lower alkyl, lower alkoxy, halo, nitro, amino, and trifluoromethyl, and that the description includes both unsubstituted phenyl and naphthyl and substituted phenyl and naphthyl.

The term "pharmaceutically-acceptable" salt means a salt of an active compound that retains the biological effectiveness of the compound and that is not pharmacologically undesirable. A pharmaceutically-acceptable acid addition salt is one prepared from an organic or inorganic acid that pairs with an appropriate base, e.g., an amino group in the active compound. Inorganic salts derived are from inorganic acids such as hydrochloric acid, hydrobromic acid, sulfuric acid, nitric acid, phosphoric acid and the like. Organic salts are derived from acids such as acetic acid, propionic acid, glycolic acid, pyruvic acid, oxalic acid, malic acid, malonic acid, succinic acid, maleic acid, fumaric acid, tartaric acid, citric acid, benzoic acid, cinnamic acid, mandelic acid, methanesulfonic acid, ethanesulfonic acid, p-toluenesulfonic acid, salicylic acid, lactic acid and the like.

The Composition

Broadly, the composition comprises a therapeutically effective amount of an antifungal compound, or a pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable excipient to provide a mixture having a consistency sufficient to adhere to the surface of a nail so that the antifungal is delivered through the nail plate. Generally the composition is a liquid or semisolid, such as a cream, ointment, lotion, or gel (preferably a gel) having a solvent in which the antifungal compound, or its salt, is dissolved. Thus, the composition will contain at least the antifungal compound, a solvent for the compound, and a gelling agent. Preferably, the composition is water-based, which means that the solvent is preferably water-miscible. In addition, the composition may include a surfactant to aid in the delivery of the antifungal through the nailplate; a keratolytic agent to aid in the loosening, disintegration or decomposition of the thickened nailplate; a film-forming agent; a buffering agent to adjust the pH of the composition; and an adherence-promoting agent to assist in adhering the composition to the nailplate. The composition may be applied directly to the nail or applied in an absorbent pad.

The antifungal compound useful in this invention is one that is effective when applied topically to treat the fungal infection. The amount of the compound present in the composition will be the amount that is therapeutically effective, i.e. an amount that will result in the effective treatment of the onychomycosis when applied in accordance with the instructions described herein. The term "treatment"

as used herein covers any treatment of onychomycosis in a mammal, particularly a human, and includes:

(i) preventing the disease from occurring in a subject which may be predisposed to the disease but has not yet been diagnosed as having it;

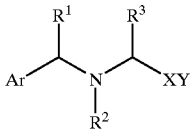
(ii) inhibiting the disease, i.e. arresting its development; and

(iii) relieving the disease, i.e. causing regression of the disease.

The therapeutically effective amount will vary depending on the subject and the severity of the affliction and may be determined routinely by one of ordinary skill in the art in light of the teaching herein. Generally, a therapeutically effective amount will be from about one-half percent by weight (0.5% wt.) to about fifteen percent by weight (15% wt.) based on the total final weight of the composition. Preferably, the amount will be about 1% to about 10% by weight and more preferably about 2% to about 8% by weight. The amount present in the composition will be dependent in part on the length of the treatment, as discussed hereinafter.

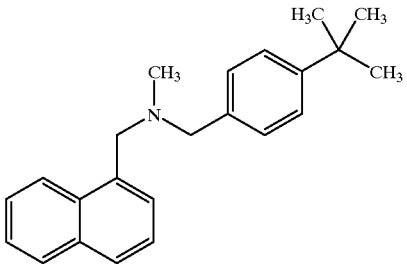
The antifungal agents of particular utility in this invention have a structure represented by Formula (I), below, and the pharmaceutically-acceptable salts thereof. These include a benzylamine moiety (for example butenafine and related compounds are disclosed in U.S. Pat. Nos. 5,021,458 and 5,106,866). Each of the foregoing patents is incorporated by reference. Antifungal of particular interest include, but are not limited to, butenafine and the pharmaceutically-acceptable salts thereof. Such compounds are represented by Formula (I) as follows:

(I)



wherein Ar is aryl; R^1 is alkil or hydrogen; R^2 is hydrogen or alkyl, R^3 is hydrogen or alkyl; X is a covalent bond; and Y is aryl or heteroaryl.

Butenafine is a preferred compound of Formula I wherein Ar is 1-naphthyl, R^1 is hydrogen, R^2 is methyl, R^3 is hydrogen, X is $—(CH_2)_n—$ in which n is 0, (i.e., a covalent bond) and Y is 4-(t-butyl)phenyl, and has the structure:



Of these compounds butenafine hydrochloride is preferred.

The pharmaceutically-acceptable solvent used in the composition of this invention is preferably miscible with water and will be present in an amount sufficient to dissolve the antifungal compound. Generally this amount will vary from about 20–80% by weight, preferably about 30% by weight to about 70% by weight, more preferably about 40% by weight to about 60% by weight. Examples of suitable solvents include pharmaceutically acceptable lower alkanols of one to four carbon atoms (e.g., ethanol, n-propanol, isopropanol, and n-butanol; preferably ethanol), pharmaceutically acceptable dihydroxylacohols (e.g., alkylene glycols such as hexylene glycol, propylene glycol, butylene glycol, and the like), benzylalcohol, propylene carbonate, polyethylene glycols (e.g., PEG 400), polypropylene glycols (e.g., PPG 725), and the like. Others may be apparent to one of ordinary skill upon reading this specification. Ethanol is preferred.

In addition to the antifungal compound and a pharmaceutically-acceptable solvent, the composition of this invention also includes a gelling agent in an amount sufficient to form a gel. Preferably the gel is a single-phase gel, i.e., it consists of organic macromolecules distributed throughout the composition in such a manner that no apparent boundaries exist between the dispersed macromolecules and the liquid. The gelling agent may be a synthetic macromolecule or a natural macromolecule, e.g., a gum, resin, polyacrylamide, mitrocellulose, or other cellulose derivatives. The gel is a semisolid preferably having a high degree of clarity, ease of application, and ease of removal. The amount of the gelling agent will vary depending on the type of solvent used, the type of gelling agent used to be appropriate with the solvent, and whether the system is aqueous or nonaqueous. Based on these considerations and others known to one of skill in the art, the gelling agent will be present in an amount from about 0.1% by weight to about 20% by weight, preferably about 0.5% by weight to about 15% by weight. Usually no more than about 10% by weight is used. Gels of this invention can be prepared from a number of pharmaceutical agents such as tragacanth about 2 to 5% wt., sodium alginate about 2 to 10% wt., gelatin about 2 to 15% wt., methylcellulose about 3 to 5% wt., sodium carboxymethylcellulose about 2 to 5% wt., carbomer about 0.3 to 5% wt., or polyvinyl alcohols about 10 to 20% wt. Other gelling agents include hydroxyethylmethyl cellulose, polyoxyethylene-polyoxypropylene block copolymers (polaxomers), ethylcellulose, and hydroxyethylcellulose. Preferably the gelling agent is chosen from methylcellulose, ethylcellulose, hydroxyethylcellulose, hydroxypropylcellulose, hydroxypropylmethylcellulose, carboxymethylcellulose and carbomer.

The gel composition of this invention is characterized by its ability to adhere to the nail being treated. Preferably, the composition will include a pharmaceutically-acceptable excipient to aid in improving adhesion properties. Certain polyurethane compounds provide superior adhesion properties and also aid in cutaneous penetration. Such a polyurethane compound would include any conventional polyurethane compound formed by reaction of a diisocyanate with a compound having an active hydrogen, for example as disclosed in U.S. Pat. No. 4,079,028 to Emmons, which is incorporated herein by reference. A compound having an active hydrogen includes alcohols, diols, triols, amines, hydroxy-terminated polyesters, silanols, carboxylic acids, and the like. More particularly, the polyurethane compound includes compounds having the formula:

$$H—[—(YR)_m—OC(O)NH—X—NHC(O)]_n—$$

$$—(YR)_m—OC(O)NH—X—NHC(O)—(RY)_m—$$

$$—[C(O)NH—X—NHC(O)O—(RY)_m—]_n—H$$

wherein:

X is an alkylene or alkenylene radical containing from 1 to about 20 carbon atoms, or a cycloalkylene or cycloalkenylene radical containing from about 5 to 20 carbon atoms, or a mononuclear or fused ring arylene radical containing from about 6 to about 10 carbon atoms, unsubstituted or substituted with one or more lower alkyl, lower alkoxy, lower alkoxy-substituted lower alkyl, nitro or arnino groups or halogen atoms;

Y is oxygen, sulfur, silicon, or —NH—;

each R is the same or different, and is chosen from alkylene, alkenylene, —SiR^2R^3—, and —CR^2R^3—NR^4—CR^2R^3—, wherein R^2, R^3 and R^4 are independently hydrogen or lower alkyl;

m is an integer selected to provide a (YR) moiety having a molecular weight of from about 40 to about 6,000; and

n and n' are the same or a different integer from 0–30 inclusive, correlated with m so as to provide a polyurethane compound having a molecular weight of up to about 200,000. Polyurethane compounds where YR is —SiR^2R^3— or —CR^2R^3—NR^4—CR^2R^3— are well known in the art (See for example U.S. Pat. No. 5,286,787 to Padolo and Majolo; U.S. Pat. No. 4,962, 178 to Harisiades; U.S. Pat. No. 4,155,892 to Emmons, et. al., and "Polyurethanes Chemistry and Technology" by J. H. Saunders and K. C. Frisch, Interscience Publishers, pp. 65–67.) Preferred are polyurethanes that are hydroxy-terminated polyurethanes, i.e. where Y is oxygen, especially those where R is alkylene or alkenylene, which are disclosed in U.S. Pat. Nos. 4,971,800, 5,045,317, and 5,051,260, the complete disclosures of which are hereby incorporated by reference. Also useful are those disclosed in U.S. Pat. 4,079,028 issued March 1978, to Emmons, et al. This, too, is incorporated herein by reference.

A preferred hydroxy-terminated polyurethane has the above formula where X is 4,4'-dicyclohexylmethane, Y is oxygen, R is 1,2-propylene, m is 1–4, n and n' are both 12. It has a tradename of polyolprepolymer-2, and is prepared by the reaction of 2 moles of polypropylene glycol and 1 mole of dicyclohexylmethane diisocyanate in the presence of stannous octoate, as detailed in U.S. Pat. No. 4,971,800, Examples 1 and 5. It has a CAS# 9042-82-4, and a CAS name poly[oxy(methyl-1,2-ethanediyl)], α-hydro-ω-hydroxy-, polymer with 1,1'-methylene-bis-[4-socyanatocyclohexane]. Also preferred is polyolprepolymer-14, which has the same CAS# and name, but a higher molecular weight (a weight average molecular weight of 14,000 as opposed to 4,000 for polyolprepolymer-2), and polyolprepolymer-15, which has a CAS# 39444-87-6, and is named poly(oxy-1,2-ethanediyl), α-hydro-ω-hydroxy-, polymer with 1,1'-methylene-bis-[4-isocyanatocyclohexane]. Generally, the optional adhesion-promoting agent will be present in an amount of 0% wt. to about 15%wt., preferably about 0.5% wt. to about 10% wt., and more preferably about 0.5% wt. to about 5% wt.

To further aid in retaining the gel composition of this invention on the surface of the nail, the composition may optionally include a film-forming agent in an amount sufficient to form a film on the surface of the gel exposed to air. Representative optional film forming agents include povidone (1-ethyenyl-2-pyrrolidone polymers, e.g., PVP K-90) polyvinyl alcohol, polyvinyl acetate, polyvinylethyl ether, polyvinyistearyl ether, vinylpyrrolidonel vinylacetate copolymers, nitrocellulose and the like. Generally, the optional film forming agent will be present in an amount of from 0% by wt. to about 5% by wt., preferably about 0.1% by wt. to about 3% by wt., more preferably about 0.1–2% by wt.

The gel composition of this invention may optionally include a surfactant to aid in the penetration of the antifungal compound through the nail plate. Representative surfactants include anionic and nonionic surfactants that are compatible with other components in the composition. Generally, the surfactant will be present in an amount of about 0% by wt to about 10% by wt., preferably about 0.5% wt to about 5% wt., more preferably about. to about 1% wt. to about 5% wt. Representatives examples of anionic surfactants include sodium lauryl sulfate, sodium laureth n-sulfate (where n is 5–12), sulfonates, sarcosinates, and sulfosuccinates. Nonionic surfactants include polysorbates, polyoxyethylene 4 lauryl ether, and the like.

The composition of this invention may optionally include a keratolytic agent, i.e., a desquamating agent, that loosen keratin in the nail and aids in the process of desquamation or the removal of the upper layers of the damaged or diseased nail. Examples of keratolytic agents include urea, benzoylperoxide, salicylic acid, resorcinol, tretinoin, and others that may be found in "Remington: The Science and Practice of Pharmacy, Nineteenth Edition, pp. 878–879. The optional keratytic agent will be present in an amount of 0% wt. to about 25% wt., preferably about 0% wt. to about 20% wt., more preferably about 1% wt. to about 20% wt.

Other excipients optionally present in the composition include a buffer for aqueous compositions to adjust the pH of the composition and a preservative. The pH will be non-irritating and is preferably adjusted to about 3.0–8.0 using an acid e.g. hydrochloric acid, phosphoric acid, lactic acid, or a base e.g. diethanolamine, triethanolamine, sodium hydroxide, or known buffering agents, e.g. phosphates such as monobasic sodium phosphate, and dibasic sodium phosphate, lactates and citrates well known in the art. A preservative may also be present, for example benzyl alcohol, sodium benzoate, methyl paraben, propyl paraben, and the like.

In summary, the gel formulation according to this invention exhibits a composition range shown in Table A.

TABLE A

	Percent Weight		
Component	Broad	Preferred	Most Preferred
Antifungal	0.5–15	1–10	2–8
Solvent	20–80	30–70	40–60
Gelling Agent	0.1–20	0.5–15	0.5–10
Adhesion-Promoting Agent	0–15	0.5–10	0.5–5
Film Forming Agent	0–5	0.1–3	0.1–2
Surfactant	0–10	0.5–5	1–5
Keratolytic Agent	0–25	0–20	1–20
Water	0–qs	qs	qs

The gel formulation according to this invention can also have a composition shown in Tables B and C.

TABLE B

Ingredients	Wt %
Water	qs
Propylene glycol	5–20
Hydroxypropylcellulose	1–5
Ethanol	20–80

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Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research

With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

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Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

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API

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LAW FIRMS
Build custom dashboards for your attorneys and clients with live data direct from the court.

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Sync your system to PACER to automate legal marketing.