Title: TRANSDERMAL DRUG DELIVERY SYSTEM WITH ACRYLATE OR METHACRYLATE FUNCTIONAL PRESSURE SENSITIVE ADHESIVE COMPOSITION

Abstract: A transdermal drug delivery system includes an active agent and a pressure sensitive adhesive composition. The active agent is for controlled transdermal delivery to the skin of a user of the system, and the pressure sensitive adhesive composition is keeping the system in contact with the skin. The pressure sensitive adhesive composition is an acrylate or methacrylate functional pressure sensitive adhesive composition that is the reaction product a pressure sensitive adhesive and a silicon-containing capping agent. That is, the silicon-containing capping agent and the pressure sensitive adhesive react to form the pressure sensitive adhesive composition. The silicon-containing capping agent comprises acrylate or methacrylate functionality and this acrylate or methacrylate functionality provides the pressure sensitive adhesive composition with its acrylate or methacrylate functionality. The pressure sensitive adhesive itself is the reaction product of a silicone resin and silicone polymer.
The present invention generally relates to a transdermal drug delivery system. More specifically, the present invention relates to a transdermal drug delivery system including a pressure sensitive adhesive composition that is the reaction product of a pressure sensitive adhesive and a silicon-containing capping agent comprising acrylate or methacrylate functionality.

Pressure sensitive adhesives, also referred to as "PSAs", are known in the art and are commercially available. Silicone pressure sensitive adhesives are typically produced by either blending or condensing together a silicone resin and a silicone polymer, such as a polydiorganosiloxane. Silicone pressure sensitive adhesives are also known in the art and are commercially available. Examples of such pressure sensitive adhesives are disclosed in United States Patent Nos. 2,736,721; 2,814,601, 2,857,356, and 3,528,940. The adhesion of such pressure sensitive adhesives can be varied by altering a ratio of M/Q units in the silicone resin or by altering a ratio of silicone resin to silicone polymer.

The use of such pressure sensitive adhesives in transdermal drug delivery systems is also known in the art. These systems typically include an active agent and a conventional pressure sensitive adhesive. The active agent, for example a pharmaceutical drug, is for controlled transdermal delivery to a substrate, such as the skin of a user of the system. The pressure sensitive adhesive maintains contact between the system and the substrate such that the active agent can be delivered to the substrate. Examples of such systems can be found in United States Patent Nos. 3,731,683; 3,797,494; 4,031,894; and 4,336,243.
As alluded to immediately above, the pressure sensitive adhesives are designed to ensure contact between the system and the substrate for an extended period of time. Ideally, the pressure sensitive adhesives, including the silicone pressure sensitive adhesives, are non-irritating and non-sensitizing to the substrate. It is known that, to maintain the stability of pressure sensitive adhesives, and therefore the stability of transdermal drug delivery systems utilizing the pressure sensitive adhesives, the pressure sensitive adhesives must contain a certain content, or concentration, of silicon bonded hydroxyl groups, i.e., silanols. In fact, the silanol content of a pressure sensitive adhesive can be adjusted based on certain factors, such as the particular type of active agent, to control the adhesiveness of the pressure sensitive adhesive. Having too much silanol content or too little silanol content can be undesirable. Also, due to the particular pressure sensitive adhesives used, the transdermal drug delivery systems of the prior art do not sufficiently optimize solubility of the active agent in the pressure sensitive adhesives. As a result, the rate at which the active agent is released from the system for delivery to the substrate and also the total amount of the active agent that is ultimately released and delivered to the substrate are not optimized in the prior art.

Pressure sensitive adhesives, including those used in the systems above, are typically provided in solution with solvent and it is known that residual silanols in the pressure sensitive adhesives can, under certain conditions, react via condensation thereby impacting the stability of these solutions. More specifically, the stability can be impacted because the viscosity of the solution tends to increase over time as a result of the condensation reaction of the residual silanols. This increase in the viscosity is undesirable, especially for long-term shelf-life. As importantly, the residual silanol content also causes loss of the adhesiveness, also referred to as a loss of tack, of the pressure sensitive adhesive.

As an example, United States Patent No. RE 35,474 teaches a transdermal drug delivery system for the controlled delivery of amino-functional drugs, as the active agent, to the substrate. It is known that amino-functional drugs interfere with the properties of pressure sensitive adhesives by catalyzing the reaction of silanol groups and, thereby, cause increased shear of the pressure sensitive adhesive and, thus, loss of
tack during storage. The ’474 patent also teaches that this effect can be inhibited by chemically treating the pressure sensitive adhesives with a treating agent which reduces their silanol content. The ’474 patent further teaches that the amount of the treating agent used to treat the pressure sensitive adhesive must be an amount of at least 0.8 moles triorganosilyl units for every mole of silanol, and that this amount of the treating agent generally reduces the silanol content of the pressure sensitive adhesive to levels below about 7700 parts per million (ppm).

However, referring now to United States Patent No. 6,337,086, it was found that when the silanol content is too low in a transdermal drug delivery system with amino-functional drugs, further crosslinking between the silicone resin and the silicone polymer can be sufficiently reduced and the resulting loosely crosslinked network becomes plasticized and oozing, thus resulting in poor quality of the pressure sensitive adhesive. The ’086 patent therefore teaches that silicone pressure sensitive adhesives having a low, but well defined content of silanol, preferably in the range of between 8,000 and 13,000 ppm, provide silicone pressure sensitive adhesives which remain useful in transdermal drug delivery systems. To accomplish the low, well defined content of silanol, the ’086 patent focuses on reducing the content of silanol with trimethylsilyl units. Relying strictly on trimethylsilyl units to reduce the content of silanol is deficient because the rate at which an active agent, such as the pharmaceutical drug, is released from the system is not optimized.

The trimethylsilyl units relied on in the ’086 patent are an example of chemically treating the respective pressure sensitive adhesives with a capping or endblocking agent to reduce their silanol content. Other examples of the use of capping or endblocking agents are disclosed in United States Patent Nos. 4,854,355; 4,858,836; 4,591,622; EP 0529840; and EP 0664328. Generally, these examples do not contemplate application of their respective pressure sensitive adhesives in transdermal drug delivery systems. As a result, these examples do not employ their respective pressure sensitive adhesives to optimize solubility of any active agent.
There remains a need to improve transdermal drug delivery systems, specifically to improve the pressure sensitive adhesives used in the transdermal drug delivery systems to optimize the rate at which the active agent is released.

**SUMMARY OF THE INVENTION**

A transdermal drug delivery system according to the present invention includes an active agent and a pressure sensitive adhesive composition. The active agent is for controlled transdermal delivery to a substrate. The pressure sensitive adhesive composition maintains contact with the substrate. The pressure sensitive adhesive composition includes the reaction product of a pressure sensitive adhesive and a silicon-containing capping agent. The pressure sensitive adhesive is the reaction product of a silicone resin and a silicone polymer. The silicon-containing capping agent comprises acrylate or methacrylate functionality.

The particular pressure sensitive adhesive composition utilized in the transdermal drug delivery system of the present invention improves a rate at which the active agent is released from the system for delivery to the substrate, i.e., improves the release rate. As a result of this improvement in the release rate, the total amount of the active agent that is ultimately released and delivered to the substrate is improved. Due to the improved release rate and the improved total delivery of the active agent, it is contemplated that less active agent in the system and/or a smaller size of the system are required which may result in significant cost savings. Finally, an additional advantage associated with this invention is that the particular silicon-containing capping agent used in the composition effectively reduces an amount of residual silanol content in the pressure sensitive adhesive as compared to the amount of residual silanol content in conventional silicone pressure sensitive adhesives. As such, the stability of the composition and of the transdermal drug delivery system is improved and adherence between the system and the substrate is maintained, which is obviously an attractive feature in transdermal drug delivery systems.
BRIEF DESCRIPTION OF THE DRAWINGS

[0012] Other advantages of the present invention will be readily appreciated, as the same becomes better understood by reference to the following detailed description when considered in connection with the accompanying drawings wherein:

[0013] Figure 1 is a line graph illustrating a release rate of 2% niacinamide in µg/cm² at various levels of acrylate post capping as compared to two controls over a time period of from 1 to 24 hours;

[0014] Figure 2 is a line graph illustrating a release rate of 2% niacinamide in µg/cm² at various levels of acrylate in situ capping as compared to two controls over a time period of from 1 to 24 hours;

[0015] Figure 3 is a line graph illustrating a release rate of 5% niacinamide in µg/cm² at various levels of acrylate post capping as compared to two controls over a time period of from 1 to 24 hours;

[0016] Figure 4 is a line graph illustrating a release rate of 5% niacinamide in µg/cm² at various levels of acrylate in situ capping as compared to two controls over a time period of from 1 to 24 hours;

[0017] Figure 5 is a line graph illustrating a release rate of 10% niacinamide in µg/cm² at various levels of acrylate post capping as compared to two controls over a time period of from 1 to 24 hours;

[0018] Figure 6 is a line graph illustrating a release rate of 10% niacinamide in µg/cm² at various levels of acrylate in situ capping as compared to two controls over a time period of from 1 to 24 hours;

[0019] Figure 7 is a line graph illustrating a release rate of 2% ketoconazole in µg/cm² at both 1% and 2.5% acrylate post capping as compared to two controls over a time period of from 1 to 24 hours;

[0020] Figure 8 is a line graph illustrating a release rate of 5% ketoconazole in µg/cm² at both 1% and 2.5% acrylate post capping as compared to two controls over a time period of from 1 to 24 hours; and
[0021] Figure 9 is a line graph illustrating a release rate of 10% ketoconazole in µg/cm² at both 1% and 2.5% acrylate post capping as compared to two controls over a time period of from 1 to 24 hours.

DETAILED DESCRIPTION

[0022] A transdermal drug delivery system includes an active agent and a pressure sensitive adhesive composition. Both the active agent and the pressure sensitive adhesive composition are described in detail below. As those skilled in the art appreciate, the system is structural and can be in many forms including, but not limited to, patches, films, multi-layer dressings, reservoir systems, and combinations thereof. The active agent is in the system for controlled transdermal delivery to a substrate. It is also possible, but not required, for the system to include a backing layer for supporting the pressure sensitive adhesive composition, and/or a release liner for protecting the pressure sensitive adhesive composition and/or the active agent prior to the controlled transdermal delivery of the active agent to the substrate. One preferred application of the transdermal drug delivery system of the present invention is to treat a user, or patient, with the active agent. As a result, the substrate is typically the skin of the user and, in this preferred application, the user applies and wears the system on their skin.

[0023] The active agent can be any component suitable for transdermal delivery to a substrate. Suitable active agents include, but are not limited to, those active agents disclosed and described in United States Patent No. 5,474,783 to Miranda et al., the disclosure of which is incorporated by reference herein in its entirety. These active agents include, but are not limited to, cardioactive medications, androgenic steroids, estrogens, hormones, progestational agents, drugs having an action on the central nervous system, nutritional agents, anti-inflammatory agents, antihistamines, respiratory agents, sympathomimetics, miotics, cholinergic agonists, antimuscarinic or muscarinic cholinergic blocking agents, mydriatics, psychicnergizers, anti-infectives, dermatological agents, humoral agents, antispasmodics, antidepressant drugs, anti-diabetic, anorectic drugs, anti-allergenics, tranquilizers, antipsychotics, decongestants, antipyretics, antimigrane agents, drugs for treating nausea and vomiting, anti-malarials,
anti-ulcerative agents, peptides, drugs for Parkinson's disease, drugs for spasticity, drugs for acute muscle spasms, anti-estrogen, anti-hormone agents, therapeutic agents, and combinations thereof.

[0024] More specific examples of the active agents outlined above that are suitable for implementation as the active agent in the present invention include:

[0025] Cardioactive medications, illustratively, organic nitrates such as nitroglycerin, isosorbide dinitrate and, isosorbide mononitrates; quinidine sulfate; procainamide; thiazides such as bendroflumethiazide, chlorothiazide, and hydrochlorothiazide; nifedipine; nicardipine; adrenergic blocking agents, such as timolol, and propranolol; verapamil; diltiazem; captopril; clonidine and prazosin;

[0026] Androgenic steroids, such as testosterone, methyltestosterone and fluoxymesterone;

[0027] Estrogens, such as, conjugated estrogens, esterified estrogens, quinestrol, estropipate, 17β-estradiol, 17β-estradiol valerate, equilin, mestranol, estrone, estriol, 17β-ethinyl estradiol, and diethylstilbestrol;

[0028] Progestational agents, such as progesterone, 19-norprogesterone, norethindrone, norethindrone acetate, melengestrol, chlormadinone, ethisterone, medroxyprogesterone acetate, hydroxyprogesterone caproate, ethynodiol diacetate, norethinodrel, 17α-hydroxyprogesterone, dydrogesterone, dimethisterone, ethinylestrenol, norgestrel, demegestone, promegestone, and megestrol acetate;

[0029] Drugs having an action on the central nervous system, for example sedatives, hyponotics, antianxiety agents, analgesics and anesthetics, such as chloral, buprenorphine, naloxone, haloperidol, fluphenazine, pentobarbital, phenobarbital, secobarbital, codeine, lidocaine, tetracaine, dyclonine, dibucaine, cocaine, procaine, mepivacaine, bupivacaine, etidocaine, prilocaine, benzocaine, fentanyl, and nicotine;

[0030] Nutritional agents, such as vitamins (e.g. niacinamide), essential amino acids and essential fats;

[0031] Anti-inflammatory agents, such as hydrocortisone, cortisone, dexamethasone, fluocinolone, triamcinolone, medrysone, prednisolone, flurandrenolide, prednisone, halcinonide, methylprednisolone, fludrocortisone, corticosterone,
paramethasone, betamethasone, ibuprofen, naproxen, fenoprofen, flurbiprofen, acetaminophen, indoprofen, ketoprofen, suprofen, indomethacin, piroxicam, aspirin, salicylic acid, diflunisal, methyl salicylate, phenylbutazone, sulindac, mefenamic acid, meclofenamate sodium, naproxen, and the like;

[0032] External analgesics, such as camphor, menthol, capsicum extract, frankincense, green tea, juniper tea, and caffeine;

[0033] Antihistamines, such as diphenhydramine, dimenhydrinate, perphenazine, triprolidine, pyrilamine, chlorcyclizine, promethazine, carboxamine, tripelennamine, brompheniramine, hydroxyzine, cyclizine, meclizine, terrenadine, and chlorpheniramine;

[0034] Respiratory agents, such as theophylline and Beta-adrenergic agonists such as albuterol, terbutaline, metaproterenol, ritodrine, carbuterol, fenoterol, quinterenol, rimiterol, solmefamol, soterenol, and tretoquinol;

[0035] Sympathomimetics such as dopamine, norepinephrine, phenylpropanolamine, phenylephrine, pseudoephedrine, amphetamine, propylhexedrine and epinephrine;

[0036] Miotics such as pilocarpine, and the like;

[0037] Cholinergic agonists, such as choline, acetylcholine, methacholine, carbachol, bethanechol, pilocarpine, muscarine, and arecoline;

[0038] Antimuscarinic or muscarinic cholinergic blocking agents, such as atropine, scopolamine, homatropine, methscopolamine, homatropine methylbromide, methantheline, cyclopentolate, tropicamide, propantheline, anisotropine, dicyclomine, and eucatropine;

[0039] Mydriatics, such as atropine, cyclopentolate, homatropine, scopolamine, tropicamide, eucatropine and hydroxyamphetamine;

[0040] Psychicenergizers, such as 3-(2-aminopropy)indole, 3-(2-amnobutyl)indole, and the like;

[0041] Anti-infectives, such as antibiotics, including penicillin, tetracycline, chloramphenicol, sulfacetamide, sulfadiazine, sulfamethoxazole and sulfisoxazole; antivirals, including idoxuridine; antibacterials, such as erythromycin and clarithromycin;
anti-fungals, such as ketoconazole, and other anti-infectives including nitrofurazone, cyclopirox, terbafine, witch hazel, and the like;

[0042] Dermatological agents, such as retinoids; vitamins C and E; benzoyl peroxide and dapsone;

[0043] Humoral agents, such as the prostaglandins, natural and synthetic, for example PGEI, PGE 2-alpha, and PGF 2-alpha, and the PGEI analog misoprostol;

[0044] Antispasmodics, such as atropine, methantheline, papaverine, cinnamedrine, and methscopolamine;

[0045] Antidepressant drugs, such as paroxetine, phenelzine, tranylcypromine, imipramine, amitriptyline, trimipramine, doxepin, desipramine, nortriptyline, protriptyline, amoxapine, maprotiline, and trazodone;

[0046] Anti-diabetics, such as insulin, and anticancer drugs such as tamoxifen and methotrexate;

[0047] Anorectic drugs, such as, dextroamphetamine, methamphetamine, phenylpropanolamine, fenfluramine, diethylpropion, mazindol, and phentermine.

[0048] Anti-allergenics, such as antazoline, methapyrilene, chlorpheniramine, pyrilamine and pheniramine;

[0049] Tranquilizers, such as reserpine, chlorpromazine, and antianxiety benzodiazepines such as alprazolam, chlor Diazepoxide, clorazepate, halazepam, oxazepam, prazepam, clonazepam, flurazepam, triazolam, lorazepam and diazepam;

[0050] Antipsychotics, such as thiopropazate, chlorpromazine, triflupromazine, mesoridazine, piperacetazine, thioridazine, acetophenazine, fluphenazine, perphenazine, trifluoperazine, chlorprothixene, thiothixene, haloperidol, bromperidol,loxapine, and molindone;

[0051] Decongestants, such as phenylephrine, ephedrine, naphazoline, tetrahydrozoline;

[0052] Antipyretics, such as aspirin, salicylamide, and the like;

[0053] Antimigrane agents, such as dihydroergotamine and pizotyline;
[0054] Drugs for treating nausea and vomiting, such as chlorpromazine, perphenazine, prochlorperazine, promethazine, triethylperazine, triflupromazine, and trimeprazine;

[0055] Anti-malarials, such as the 4-aminoquinolines, alphaaminoquinolines, chloroquine, and pyrimethamine;

[0056] Anti-ulcerative agents, such as misoprostol, omeprazole, and enprostil;

[0057] Peptides, such as growth releasing factor;

[0058] Drugs for Parkinson’s disease, spasticity, and acute muscle spasms such as levodopa, carbidopa, amantadine, apomorphine, bromocriptine, selegiline (deprenyl), trihexyphenidyl hydrochloride, benztpine mesylate, procyclidine hydrochloride, baclofen, diazepam, and dantrolene; and

[0059] Anti-estrogen or hormone agents, such as tamoxifen or human chorionic gonadotropin.

[0060] As indicated above, the particular active agent is not limited to those recited above. Other examples of suitable active agents for use in the systems will be apparent to those skilled in the art (See, for example, pages 149-217 of Yie Chien’s treatise entitled “Novel Drug Delivery Systems” which is Volume 14 of Drugs and the Pharmaceutical Sciences, Marcel Dekker, Inc., New York, NY. 10016 (1982)).

[0061] As those skilled in the art appreciate, the active agents can be present in the system in different forms, depending on which form yields optimum delivery characteristic, such as the release rate and the total amount released as described below. For example, in the case of drugs, the drug can be in its free base or acid form, or in the form of salts, esters, or any other pharmacologically acceptable derivatives, or even as components of molecular complexes.

[0062] The amount of the active agent incorporated into the system varies depending on many factors including, but not limited to, the particular active agent, the desired therapeutic effect, and the time span for which the system is to provide therapy. For most active agents, the passage of the active agent through the skin is the rate-limiting step in transdermal delivery. Thus, the amount of the active agent and the rate of release are typically selected so as to provide transdermal delivery characterized by a
zero order time dependency for a prolonged period of time. The minimum amount of active agent in the system is selected based on the amount of active agent which passes through the skin, or other substrate, in the time span for which the system is to provide therapy. Preferably, the amount of active agent in the system varies from about 0.1% up to about 60% by weight of the system, more preferably from about 0.3% up to about 50% by weight of the system, and for the lower drug doses permitted by this invention, most preferably from about 1.0% up to about 30% by weight of the system. The weight of the system is, at a minimum, the combined weight of the active agent and the pressure sensitive adhesive composition.

[0063] Furthermore, relative to the active agent, it is to be recognized that the active agent is most typically disposed in the pressure sensitive adhesive composition. However, it is also to be understood that the active agent and said pressure sensitive adhesive composition may coexist in the system in discrete layers. That is, in certain embodiments, the active agent is not disposed, or directly incorporated, into the pressure sensitive adhesive composition.

[0064] Of course, the transdermal drug delivery system can also contain other agents known to accelerate the delivery of the active agent through the skin or other substrate. These other agents are also referred to in the art as skin-penetration or permeation enhancers, accelerants, adjuvants, and sorption promoters, and are collectively referred herein simply as "enhancers". These enhancers includes those with diverse mechanisms of action including those which have the function of improving the solubility and diffusibility of the active agent within the pressure sensitive adhesive composition and those which improve percutaneous absorption, for example, by changing the ability of the stratum corneum to retain moisture, softening the skin, improving the skin's permeability, acting as penetration assistants or hair-follicle openers or changing the state of the skin including the boundary layer. Some of these enhancers have more than one mechanism of action, but in essence they serve to enhance the delivery of the active agent to the substrate.

[0065] Some examples of enhancers are polyhydric alcohols such as dipropylene glycol, propylene glycol, and polyethylene glycol which enhance solubility of the active
agent, oils such as olive oil, squalene, and lanolin; fatty ethers such as cetyl ether and oleyl ether; fatty acid esters such as isopropyl myristate which enhance diffusibility of the active agent; urea and urea derivatives such as allantoin which affect the ability of keratin to retain moisture; polar solvents such as dimethyldecylphosphoxide, methylloctylsulfoxide, dimethyllaurylamide, dodecylpyrrolidone, isosorbitol, dimethylacetonide, dimethylsulfoxide, decylmethylsulfoxide, and dimethylformamide which affect keratin permeability; salicylic acid which softens the keratin; amino acids which are penetration assistants; benzyl nicotinate which is a hair follicle opener; and higher molecular weight aliphatic surfactants such as lauryl sulfate salts which change the surface state of the substrate, e.g. skin, and the active agents administered. Other agents include oleic and linoleic acids, ascorbic acid, panthenol, butylated hydroxytoluene, tocopherol, tocopheryl acetate, tocopheryl linoleate, propyl oleate, and isopropyl palmitate.

[0066] In certain embodiments of the invention, a plasticizer or tackifying agent may be incorporated into the system, preferably into the composition, to improve the adhesive characteristics of the pressure sensitive adhesive composition. A tackifying agent is particularly useful in those embodiments in which the active agent does not plasticize the silicone polymer. Suitable tackifying agents are those known in the art including: (1) aliphatic hydrocarbons; (2) mixed aliphatic and aromatic hydrocarbons; (3) aromatic hydrocarbons; (4) substituted aromatic hydrocarbons; (5) hydrogenated esters; (6) polyterpenes; and (7) hydrogenated wood rosins. The tackifying agent employed is preferably compatible with the other components in the composition. Examples of suitable tackifying agents are silicone fluid (e.g., Q7-9120 Silicone Fluid, available from Dow Corning Corporation, Midland, Michigan) or mineral oil. Silicone fluid is useful for blends comprising polysiloxane as a major component. In other embodiments, where a synthetic rubber, for example, is a major component, mineral oil is a useful tackifying agent.

[0067] Notably some active agents, such as vasodilator nitroglycerin, function as plasticizers in the composition because they are soluble to a certain degree in the components of the composition. For active agents which are not readily soluble in the in
the components, a co-solvent for the active agent and other components can be added. Co-solvents, such as lecithin, retinol derivatives, tocopherol, dipropylene glycol, triacetin, propylene glycol, saturated and unsaturated fatty acids, mineral oil, silicone fluid, alcohols, butyl benzyl phthalate, and the like are useful in the practice of the instant invention depending on the solubility of the active agent in the composition.

Independent of, or in conjunction with, the tackifying agent, the pressure sensitive adhesive composition maintains contact between the system and the substrate. The pressure sensitive adhesive composition, also referred to throughout simply as the composition, is an adhesive that possesses sufficient tack and cohesive strength so that it can be adhered with mild pressure and also removed and the adhered again (to the same or another). The pressure sensitive adhesive composition more specifically includes the reaction product of a pressure sensitive adhesive and a silicon-containing capping agent. In other words, the silicon-containing capping agent and the pressure sensitive adhesive reaction to form the composition. The silicon-containing capping agent comprises acrylate or methacrylate functionality and is described additionally below.

Although not required, the pressure sensitive adhesive is preferably present in the composition in an amount of from 85.0 to 99.9 parts by weight based on weight % solids of the pressure sensitive adhesive, and the silicon-containing capping agent is preferably present in the composition in an amount of from 0.1 to 15 parts by weight based on weight % solids of the pressure sensitive adhesive. More preferably, the pressure sensitive adhesive is present in the composition in an amount of from 85.0 to 99.8 parts by weight based on weight % solids of the pressure sensitive adhesive, and the silicon-containing capping agent is present in the composition in an amount of from 0.2 to 15 parts by weight based on weight % solids of the pressure sensitive adhesive. Most preferably, the pressure sensitive adhesive is present in the composition in an amount of from 90.0 to 99.25 parts by weight based on weight % solids of the pressure sensitive adhesive, and the silicon-containing capping agent is more preferably present in the composition in an amount of from 0.75 to 10 parts by weight based on weight % solids of the pressure sensitive adhesive. In further embodiments, the pressure sensitive adhesive is present in the composition is present in the composition in an amount of from 85.0 to
99.5 parts by weight based on weight % solids of the pressure sensitive adhesive, and the silicon-containing capping agent is present in the composition in an amount of from 0.5 to 15 parts by weight based on weight % solids of the pressure sensitive adhesive. In yet further embodiments, the pressure sensitive adhesive is present in the composition in an amount of from 85.0 to 99.25 parts by weight based on weight % solids of the pressure sensitive adhesive, and the silicon-containing capping agent is present in the composition in an amount of from 0.75 to 15 parts by weight based on weight % solids of the pressure sensitive adhesive. Typically, the pressure sensitive adhesive has a weight % solids of from 50 to 65%, more typically 60%.

The pressure sensitive adhesive includes the reaction product of a silicone resin and a silicone polymer. Preferably, the silicone resin reacts in an amount of from 40 to 70 parts by weight to form the pressure sensitive adhesive, and the silicone polymer reacts in an amount of from 30 to 60 parts by weight to form the pressure sensitive adhesive. Both of these parts by weight are based on 100 parts by weight of the pressure sensitive adhesive. Although not required, the pressure sensitive adhesive may comprise a catalytic amount of a condensation catalyst. Those skilled in the art readily appreciate the wide variety of catalysts that can be used to catalyze condensation between the silicone resin and the silicone polymer. Typically, these catalysts are simple bases or acids. One, non-limiting examples of such a condensation catalyst is potassium hydroxide. Of course, the catalytic amount of the condensation catalyst varies based on a wide variety of factors including, but not limited to, the particular condensation catalyst, the particular silicone resin, and the particular silicone polymer used.

There is a wide array of silicone resins and silicone polymers that are suitable to make up the pressure sensitive adhesive. Suitable silicone resins and silicone polymers include, but are not limited to, those disclosed and described in United States Patent No. 6,337,086 to Kanios et al., the disclosure of which is incorporated by reference herein in its entirety.

A preferred silicone resin comprises a copolymer comprising triorganosiloxy units of the formula \( R^3 SiO_{122} \) and tetrafunctional siloxy units of the formula \( SiO_{4} \) in a ratio of about 0.6 to 0.9 triorganosiloxy units for each tetrafunctional
siloxy unit, wherein each R³ independently denotes a monovalent hydrocarbon radical having from 1 to 6 carbon atoms, and a preferred silicone polymer comprises at least one polydiorganosiloxane comprising AR³SiO units terminated with endblocking TR³ASiO½ units, wherein the polydiorganosiloxane has a viscosity of from about 100 centipoise to about 30,000,000 centipoise at 25°C, each A radical is independently selected from R³ or halohydro-carbon radicals having from 1 to 6 carbon atoms, each T radical is independently selected from the group consisting of R³, OH, H or OR⁴, and each R⁴ is independently an alkyl radical having from 1 to 4 carbon atoms.

As an example using forms of this preferred silicone resin and this preferred silicone polymer, one type of pressure sensitive adhesive is made by:

mixing (i) from 40 to 70 inclusive parts by weight of at least one resin copolymer containing silicon-bonded hydroxyl radicals and consisting essentially of R³SiO½ units and SiO₄½ units in a mole ratio of 0.6 to 0.9 R³SiO½ units for each SiO₄½ unit present, (ii) between about 30 and about 60 parts by weight of at least one polydiorganosiloxane comprising AR³SiO units terminated with endblocking TR³ASiO½ units, wherein the polydiorganosiloxane has a viscosity of from about 100 centipoise to about 30,000,000 centipoise at 25°C and each R³ is a monovalent organic radical selected from the group consisting of hydrocarbon radicals of from 1 to 6 inclusive carbon atoms, each A radical is independently selected from R³ or halohydrocarbon radicals having from 1 to 6 inclusive carbon atoms, each T radical is independently selected from the group consisting of R³, OH, H or OR⁴, and each R⁴ is independently an alkyl radical of from 1 to 4 inclusive carbon atoms; a sufficient amount of (iii) at least one of the silicon-containing capping agents described below and capable of providing a silanol content, or concentration, in the range of 5,000 to 15,000, more typically 8,000 to 13,000, ppm, when desirable an additional catalytic amount of (iv) a mild silanol condensation catalyst in the event that none is provided by (ii), and when necessary, an effective mount of (v) an organic solvent which is inert with respect to (i), (ii), (iii) and (iv) to reduce the viscosity of a mixture of (i), (ii), (iii), and (iv), and condensing the mixture of (i), (ii), (iii) and (iv) at least until a substantial amount of the silicon-containing capping agent or agents have reacted with the silicon-
bonded hydroxyl radicals and T radicals of (i) and (ii). Additional organosilicon endblocking agents can be used in conjunction with the silicon-containing capping agent or agents (iii) of the present invention. Such additional organosilicon endblocking agents, also referred to herein as a second silicon-containing capping agent, are described additionally below.

[0076] The pressure sensitive adhesives are made in accordance with the present invention using from 40 to 70 inclusive parts by weight of silicone copolymer resins (i) and from 30 to 60 parts by weight of polydiorganosiloxane (ii) of the type which have been used in the past to make such adhesives. More preferred are compositions employing from 50 to 65 parts by weight of resin copolymer (i) and from 35 to 50 parts by weight of polydiorganosiloxane (ii).

[0077] The silicone resin copolymers (i) are well-known materials. They contain silicon-bonded hydroxyl radicals in amounts which typically range from about 1 to 4 weight percent of silicon-bonded hydroxyl radicals and comprise triorganosiloxy units of the formula $\text{R}^3\text{SiO}_{1/2}$ and tetrafunctional siloxy units of the formula $\text{SiO}_{4/2}$ in a mole ratio of from 0.6 to 0.9 $\text{R}^3\text{SiO}_{4/2}$ units for each $\text{SiO}_{4/2}$ unit present. Blends of two or more such copolymers may also be used. There should be at least some and preferably at least 0.5% silicon-bonded hydroxyl content to enable the polydiorganosiloxane component to copolymerize with the copolymer resin and/or to react with the endblocking agent being added to chemically treat the silicone pressure-sensitive adhesive. These resin copolymers are generally benzene-soluble resinous materials which are typically solids at room temperature and are prepared as, and usually, but not necessarily used as, a solution in an organic solvent. Typical organic solvents used to dissolve resin copolymer (i) include benzene, toluene, xylene, methylene chloride, perchloroethylene, naphtha mineral spirits and mixtures of these.

[0078] Resin copolymer (i) consists essentially of from 0.6 to 0.9 $\text{R}^3\text{SiO}_{1/2}$ units for every $\text{SiO}_{4/2}$ unit in the copolymer. There may also be a few mole percent of $\text{R}^3\text{SiO}$ units present in the copolymer provided that the presence of such units does not cause the ultimate product of this process to lose its ability to function as a PSA. Each $\text{R}^3$ denotes, independently, a monovalent hydrocarbon radical having from 1 to 6 inclusive carbon
atoms such as methyl, ethyl, propyl, isopropyl, hexyl, cyclohexyl, vinyl, allyl, propenyl and phenyl. Preferably, the $R^3SiO_{2/y}$ units are $Me_3SiO_{2/y}$ units and $Me_2R^1SiO_{2/y}$ units wherein is $R^1$ is a vinyl ("Vi") or phenyl ("Ph") radical. More preferably, no more than 10 mole percent of the $R^3SiO_{2/y}$ units present in resin copolymer (i) are $Me_2R^2SiO_{2/y}$ units and the remaining units are $Me_3SiO_{2/y}$ units where each $R^2$ is a vinyl radical. Most preferably, the $R^3SiO_{2/y}$ units are $Me_3SiO_{2/y}$ units.

The mole ratio of $R^3SiO_{2/y}$ and $SiO_{4/2}$ units can be determined simply from a knowledge of the identity of the $R^3$ radicals in the $R^3SiO_{2/y}$ units and the percent carbon analysis of the resin copolymer. In the preferred resin copolymer consisting of from 0.6 to 0.9 $Me_3SiO_{2/y}$ units for every $SiO_{4/2}$ unit, the carbon analysis has a value of from 19.8 to 24.4 percent by weight.

Resin copolymer (i) may be prepared according to Daudt et al., U.S. Pat. No. 2,676,182 (issued Apr. 20, 1954 and hereby incorporated by reference) whereby a silica hydrosol is treated at a low pH with a source of $R^3SiO_{2/y}$ units such as a hexaorganodisiloxane such as $Me_3SiOSiMe_3$, $ViMe_2SiOSiMe_2Vi$ or $MeViPhSiOSiPhViMe$ or triorganosilane such as $Me_3SiCl$, $Me_2ViSiCl$ or $MeViPhSiCl$. Such copolymer resins are typically made such that the copolymer resin contains about 1 to 4 weight percent of silicon-bonded hydroxyl radicals. Alternatively, a mixture of suitable hydrolyzable silanes free of $R^3$ radicals may be cohydrolyzed and condensed. In this alternative procedure, it is a typical practice to further treat the copolymer product with a suitable silylating agent, such as hexamethyldisilazane or divinyltetramethyldisilazane, to reduce the silicon-bonded hydroxyl content of the copolymer product to less than 1 percent by weight. This step would not be necessary, but could be used, in the process now being described. Preferably, the resin copolymers employed contain from about 1 to 4 weight percent of silicon-bonded hydroxyl radicals.

Ingredient (ii) is also a well-known material and is one or more polydiorganosiloxanes comprising $AR^3SiO$ units terminated with endblocking $TR^3ASiO1/2$ units, each of which polydiorganosiloxanes has a viscosity of from 100 centipoise to 30,000,000 centipoise at 25°C (100 millipascal-seconds to 30,000 pascal seconds (Pa.s)) where 1 centipoise equals 1 millipascal second). As is well-known,
viscosity is directly related to the average number of diorganosiloxane units present for a series of polydiorganosiloxanes of varying molecular weights which have the same endblocking units. Polydiorganosiloxanes having a viscosity of from about 100 to 100,000 centipoise at 25°C range from fluids to somewhat viscous polymers. These polydiorganosiloxanes are preferably prereacted with resin copolymer (i) prior to condensation in the presence of endblocking agent (iii) to improve the tack and adhesion properties of the resulting PSA as will be further described. Polydiorganosiloxanes having viscosities in excess of 100,000 centipoise can typically be subjected to the condensation/endblocking step (II) of the present invention without prereaction. Polydiorganosiloxanes having viscosities in excess of 1,000,000 centipoise are highly viscous products often referred to as gums and the viscosity is often expressed in terms of a Williams Plasticity value (polydimethylsiloxane gums of about 10,000,000 centipoise viscosity typically have a Williams Plasticity Value of about 50 mils (1.27 mm) or more at 25°C).  

[0082] The polydiorganosiloxanes of (ii) consist essentially of AR\(^3\)SiO units where each R\(^3\) is as defined above. Each A radical is selected from radicals such as R\(^3\) or halohydrocarbon radicals of from 1 to 6 inclusive carbon atoms such as chloromethyl, chloropropyl, 1-chloro-2-methylpropyl, 3,3,3-trifluoropropyl and F\(_3\)C(CH\(_2\)_15 radicals. Thus the polydiorganosiloxane can contain Me\(_2\)SiO units, PhMeSiO units, MeViSiO units, Ph\(_2\)SiO units, methylethylsiloxy units, 3,3,3-trifluoropropyl units and 1-chloro, 2-methylpropyl units and the like. Preferably, the AR\(^3\)SiO units are selected from the group consisting of R\(^3\)\(_2\)SiOR \(^3\)R\(^4\)SiO units, Ph\(_2\)SiO units and combinations of both where R\(^3\) and R\(^4\) are as above, at least 50 mole percent of the R\(^4\) radicals present in the polydiorganosiloxane (ii) are methyl radicals and no more than 50 mole percent of the total moles of AR\(^3\)SiO units present in each polydiorganosiloxane of (ii) are Ph\(_2\)SiO units. More preferably, no more than 10 mole percent of the AR\(^3\)SiO units present in each polydiorganosiloxane (ii) are MeR\(^3\)SiO units where R\(^3\) is as above defined and the remaining AR\(^3\)SiO units present in each polydiorganosiloxane are Me\(_2\)SiO units. Most preferably, substantially all of the AR\(^3\)SiO units are Me\(_2\)SiO units,
Each polydiorganosiloxane (ii) is terminated with endblocking units of the unit formula TR\(^3\)ASiO\(_{1/2}\) where R\(^3\) and A are as defined above and each T radical is R\(^3\), OH, H or OR\(^4\) radicals where each R\(^4\) is an alkyl radical of from 1 to 4 inclusive carbon atoms such as methyl, ethyl, n-propyl, and isobutyl radicals, H, OH and OR\(^4\) provide a site for reaction with the acrylate or methacrylate functional silicon-containing capping agent of the present invention (iii) and also provide a site for condensation with other such radicals on polydiorganosiloxanes (ii) or with the silicon-bonded hydroxyl groups present in resin copolymer (i). Use of polydiorganosiloxanes where T is OH is most preferred because the polydiorganosiloxane (ii) can then readily copolymerize with the resin copolymer (i). When an appropriate catalyst such as HCl, which is generated when chlorosilanes are used, or ammonia, which is generated when organosilazanes are used as endblocking agents, then triorganosiloxyl (e.g., R\(^3\)SiOi/\(_2\)) such as (CH\(_3\))\(_3\)SiOi/\(_2\) or CH\(_2\)CH(CH\(_3\))\(_2\) SiOy/\(_2\) unit terminated polydiorganosiloxanes can be employed because some of the triorganosiloxyl units can be cleaved when the condensation reaction is conducted with heating. The cleavage exposes a silicon-bonded hydroxyl radical which can then condense with silicon-bonded hydroxyl radicals in the copolymer resin, with endblocking triorganosilyl units or with other polydiorganosiloxanes containing H, OH or OR\(^4\) radicals or silicon-bonded hydroxyl radicals exposed by cleavage reactions. Mixtures of polydiorganosiloxanes containing different substituent radicals may also be used.

Methods for the manufacture of such polydiorganosiloxanes are well known as exemplified by the following U.S. Patent Nos.: 2,490,357 (Hyde); 2,542,334 (Hyde); 2,927,907 (Polmanteer); 3,002,951 (Johannson); 3,161,614 (Brown, et al.); 3,186,967 (Nitzche, et al.); 3,509,191 (Atwell), and 3,697,473 (Polmanteer, et al.) which are hereby incorporated by reference.

To obtain PSAs which are to be cured by peroxide or through aliphatically unsaturated radicals present in resin copolymer (i) or polydiorganosiloxane (ii), if resin copolymer (i) contains aliphatically unsaturated radicals, then polydiorganosiloxane (ii) should be free of such radicals and vice-versa. If both components contain aliphatically
unsaturated radicals, curing through such radicals can result in products which do not act as PSAs.

[0086] As alluded to above, the pressure sensitive adhesive comprises a concentration of silicon bonded hydroxyl groups (i.e., silanols) and the silicon-containing capping agent is further defined as an endblocking agent. The terms endblocking agents and capping agents are used interchangeably throughout the art and in the subject description. The endblocking agent and the pressure sensitive adhesive are condensed to produce the pressure sensitive adhesive composition. More specifically, the endblocking agent reacts with the concentration of silicon bonded hydroxyl groups to cap the pressure sensitive adhesive. As generally alluded to above, once the endblocking agent reacts with the pressure sensitive adhesive, the concentration of silanols in the composition is from 5,000 to 15,000, more typically from 8,000 to 13,000, ppm.

[0087] The endblocking agent can be introduced to react with the pressure sensitive adhesive after the pressure sensitive adhesive has already been formed, i.e., after the silicone resin and the silicone polymer which make up the pressure sensitive adhesive have reacted. This technique may be generally referred to as post capping. Alternatively, the endblocking agent can be reacted in situ with the silicone resin and the silicone polymer such that the endblocking agent is present as the silicone resin and the silicone polymer are reacting. That is, the endblocking agent is introduced either prior to or during the reaction of the silicone resin and the silicone polymer. In either case, the silicone resin and the silicone polymer are reacted in the presence of the silicon-containing capping agent.

[0088] In a preferred embodiment of the present invention, the silicon-containing capping agent is selected from the group of acrylate functional silanes, acrylate functional silazanes, acrylate functional disilazanes, acrylate functional disiloxanes, methacrylate functional silanes, methacrylate functional silazanes, methacrylate functional disilazanes, methacrylate functional disiloxanes, and combinations thereof.

[0089] Alternatively, the endblocking agent may be described to be of the general formula (XYR₂Si)₂D wherein X is a monovalent radical of the general formula AE- where E is -O- or -NH- and A is an acryl group or a methacryl group, Y is a divalent
alkylene radical having from 1 to 6 carbon atoms, R is a methyl or a phenyl radical, and D is a divalent or a trivalent organic hydrolyzable radical. Preferably, D is -O- or -NH-. Most preferably, this particular endblocking agent is selected from the group of Bis(3-methacryloxypropyl)tetramethyldisilazane, Bis(3-acryloxypropyl)tetramethyldisilazane, Bis(3-methacryloxypropyl)tetramethyldisiloxane, Bis(3-acryloxypropyl)tetramethyldisiloxane, and combinations thereof.

[0090] The acryl group provides the silicon-containing capping agent with acrylate functionality and the methacryl group provides the silicon-containing capping agent with the methacrylate functionality. Those skilled in the art recognize that the acryl group can be generically represented as

\[ \text{H}_2\text{C} = \text{C} \text{-} \text{O} \]

[0091] The methacryl group can be generally represented as

\[ \text{H}_2\text{C} = \text{C} \text{-} \text{O} \]

[0092] Even further, the endblocking agent may be described to be of the general formula \( \text{XYR'}_b\text{SiZ}_{1-b} \) wherein X is a monovalent radical of the general formula AE- where E is -O- or -NH- and A is an acryl group or a methacryl group as set forth above, Y is a divalent alkylene radical having from 1 to 6 carbon atoms, R' is a methyl or a phenyl radical, Z is a monovalent hydrolyzable organic radical or a halogen, and b is 0, 1, or 2. Preferably, the monovalent hydrolyzable organic radical is of the general formula R"O- where R" is an alkylene radical. Most preferably, this particular endblocking agent is selected from the group of 3-methacryloxypropyldimethylchlorosilane, 3-methacryloxypropyldichlorosilane, 3-methacryloxypropyltrichlorosilane, and combinations thereof.

...
methacryloxypropyldimethylmethoxysilane, 3-methacryloxypropylmethyldimethoxysilane, 3-methacryloxypropyltrimethoxysilane, 3-methacryloxypropyldimethylethoxysilane, 3-methacryloxypropylmethyldiethoxysilane, 3-methacryloxypropyltriethoxysilane, (methacryloxymethyl)dimethylmethoxysilane, (methacryloxymethyl)metlyldimethoxysilane, (methacryloxymethyl)trimethoxysilane, (methacryloxymethyl)methyldimethoxysilane, (methacryloxymethyl)methyldiethoxysilane, (methacryloxymethyl)triethoxysilane, methacryloxymethyltriethoxysilane, methacryloxypropyltriisopropoxy silane, 3-acryloxypropyltrimethylsilazane, [0093] As alluded to above, the second silicon-containing capping agent can be used in conjunction with the silicon-containing capping, or endblocking, agent of the present invention. This second silicon-containing capping agent is distinguishable from the silicon-containing capping agent in that the second silicon-containing capping agent is free of acrylate and methacrylate functionality. If included, the second silicon-containing capping agent, an organosilicon endblocking agent, is along with the silicon-containing capping agent and the pressure sensitive adhesive a reaction product that forms the composition. The second silicon-containing capping agent is capable of generating an endblocking triorganosilyl unit. Suitable second silicon-containing capping agents include, but are not limited to, those described in United States Patent No. 6,337,086 to Kanios et al., the disclosure of which has already been incorporated by reference in its entirety.

[0094] Two of the active agents described above are niacinamide and ketoconazole. When the active agent comprises niacinamide in amount of 1.5 to 2.5, preferably 2, parts by weight based on 100 parts by weight of the system and the silicon-containing capping agent is post capped, the niacinamide is released from the system at a rate of 50 to 350, preferably 75 to 300, µg/cm² over a time period of 1 to 24 hours. This particular release rate is illustrated in Figure 1 and spans acrylate capping levels from 0.5
to 5% by weight solids of PSA. When the active agent comprises niacinamide in amount of 1.5 to 2.5, preferably 2, parts by weight based on 100 parts by weight of the system and the silicon-containing capping agent is capped in situ, the niacinamide is released from the system at a rate of 50 to 500, preferably 65 to 450, μg/cm² over a time period of 1 to 24 hours. This particular release rate is illustrated in Figure 2 and spans acrylate capping levels from 0.5 to 5% by weight solids of PSA.

[0095] When the active agent comprises niacinamide in amount of 4 to 6, preferably 5, parts by weight based on 100 parts by weight of the system and the silicon-containing capping agent is post capped, the niacinamide is released from the system at a rate of 170 to 800, preferably 200 to 750, μg/cm² over a time period of 1 to 24 hours. This particular release rate is illustrated in Figure 3 and spans acrylate capping levels from 0.5 to 5% by weight solids of PSA. When the active agent comprises niacinamide in amount of 4 to 6, preferably 5, parts by weight based on 100 parts by weight of the system and the silicon-containing capping agent is capped in situ, the niacinamide is released from the system at a rate of 150 to 1000, preferably 200 to 875, μg/cm² over a time period of 1 to 24 hours. This particular release rate is illustrated in Figure 4 and spans acrylate capping levels from 0.5 to 5% by weight solids of PSA.

[0096] When the active agent comprises niacinamide in amount of 7 to 13, preferably 10, parts by weight based on 100 parts by weight of the system and the silicon-containing capping agent is post capped, the niacinamide is released from the system at a rate of 250 to 1300, preferably 300 to 1250, μg/cm² over a time period of 1 to 24 hours. This particular release rate is illustrated in Figure 5 and spans acrylate capping levels from 0.5 to 5% by weight solids of PSA. When the active agent comprises niacinamide in amount of 7 to 13, preferably 10, parts by weight based on 100 parts by weight of the system and the silicon-containing capping agent is capped in situ, the niacinamide is released from the system at a rate of 300 to 1500, preferably 350 to 1400, μg/cm² over a time period of 1 to 24 hours. This particular release rate is illustrated in Figure 6 and spans acrylate capping levels from 0.5 to 5% by weight solids of PSA.
When the active agent comprises ketoconazole in amount of 1.5 to 2.5, preferably 2, parts by weight based on 100 parts by weight of the system and the silicon-containing capping agent is post capped, the ketoconazole is released from the system at a rate of 5 to 90, preferably 7 to 80, µg/cm² over a time period of 1 to 24 hours. This particular release rate is illustrated in Figure 7 and includes acrylate capping levels of 1% and 2.5% by weight solids of PSA. When the active agent comprises ketoconazole in amount of 4 to 6, preferably 5, parts by weight based on 100 parts by weight of the system and the silicon-containing capping agent is post capped, the ketoconazole is released from the system at a rate of from 4 to 90, preferably 6 to 80, µg/cm² over a time period of 1 to 24 hours. This particular release rate is illustrated in Figure 8 and includes acrylate capping levels of 1% and 2.5% by weight solids of PSA. When the active agent comprises ketoconazole in amount of 7 to 13, preferably 10, parts by weight based on 100 parts by weight of the system and the silicon-containing capping agent is post capped, the ketoconazole is released from the system at a rate of 6 to 90, preferably 7 to 80, µg/cm² over a time period of 1 to 24 hours. This particular release rate is illustrated in Figure 9 and includes acrylate capping levels of 1% and 2.5% by weight solids of PSA.

EXAMPLES

The following Examples illustrating specifics associated with pressure sensitive adhesive composition according to the subject invention, as presented herein, are intended to illustrate and not limit the invention. In the following Examples, all parts and percentages are on a by weight basis, unless otherwise indicated.

Control Example 1 (PSA 1)

Control Example 1, also referred to below as PSA 1, is a conventional, i.e., uncapped, silicone PSA that is produced through a condensation reaction of a silanol endblocked polydimethylsiloxane (PDMS) with a silicate resin and that is 60% solids in ethyl acetate.

Control Example 2
Control Example 2 is an amine-compatible, silicone PSA that is produced through a condensation reaction of a silanol endblocked polydimethylsiloxane (PDMS) with a silicate resin and that is fully capped with trimethylsiloxy groups and is 60% solids in ethyl acetate.

Example 1 - Post Capping / 0.5% Acrylate capping by weight solids of PSA

To a 32 ounce jar, 840.0 g of PSA 1 and 2.52 g of CA-I were added. Generation of HCl was immediate as indicated by pH paper color change. Material was allowed to mix overnight on a mixing wheel. The next day, 150 g of sodium bicarbonate was added to the material to aid in the neutralization of the HCl. Sample was allowed to mix overnight. The pressure sensitive adhesive composition was then pressure filtered the next day to remove particulate.

Example 2 - Post Capping / 0.75% Acrylate capping by weight solids of PSA

To a 32 ounce jar, 840.0 g of PSA 1 and 3.78 g of CA-I were added. Generation of HCl was immediate as indicated by pH paper color change. Material was allowed to mix overnight on a mixing wheel. The next day, 150 g of sodium bicarbonate was added to the material to aid in the neutralization of the HCl. Sample was allowed to mix overnight. The pressure sensitive adhesive composition was then pressure filtered the next day to remove particulate.

Example 3 - Post Capping / 1.0% Acrylate capping by weight solids of PSA

To a 32 ounce jar, 833.5 g of PSA 1 and 5.0 g of CA-I were added. Generation of HCl was immediate as indicated by pH paper color change. Material was allowed to mix overnight on a mixing wheel. The next day, 126 g of sodium bicarbonate was added to the material to aid in the neutralization of the HCl. Sample was allowed to mix overnight. The pressure sensitive adhesive composition was then pressure filtered the next day to remove particulate.

Example 4 - Post Capping / 2.5% Acrylate capping by weight solids of PSA

To a 32 ounce jar, 833.2 g of PSA 1 and 12.5 g of CA-I were added. Generation of HCl was immediate as indicated by pH paper color change. Material was allowed to mix overnight on a mixing wheel. The next day, 125 g of sodium bicarbonate
was added to the material to aid in the neutralization of the HCl. Sample was allowed to mix overnight. The pressure sensitive adhesive composition was then pressure filtered the next day to remove particulate.

Example 5 - Post Capping / 5.0% Acrylate capping by weight solids of PSA

To a 32 ounce jar, 500.0 g of PSA 1 and 15.0 g of CA-I were added. Generation of HCl was immediate as indicated by pH paper color change. Material was allowed to mix overnight on a mixing wheel. The next day, 100 g of sodium bicarbonate was added to the material to aid in the neutralization of the HCl. Sample was allowed to mix overnight. The pressure sensitive adhesive composition was then pressure filtered the next day to remove particulate.

Example 6 - In Situ Capping / 0.5% Acrylate capping by weight solids of PSA

274.43 g of Resin-1 (71.79% solids solution in xylene comprising trimethylsiloxyl and hydroxy end-blocked silicate resin in a three dimensional structure), 161.19 g of Polymer- 1 (hydroxy end-blocked polydimethylsiloxane with a viscosity of 13,500 cp at 25°C and non-volatile content minimum of 99%) and 162.58 g of xylene were blended together to yield a nominal 60% solids mixture. The mixture was placed into a glass reactor and 1.8 g of CA-2 were added to this mixture. The reactor was equipped with a bottom discharge, thermometer, nitrogen inlet, Dean-Starke trap, water-cooled condenser, a stirring paddle and a heating mantle. Under mixing and a nitrogen purge, the reactor was heated to 145°C. A condensation catalyst, anhydrous ammonia, was bubbled through the reaction mixture. As the material started to condense, water was collected as an azeotrope in the Dean-Starke trap. The reaction was continued for 4 hours at which time the addition of ammonia was discontinued. The mixture was allowed to continue to reflux at 145°C to remove any residual ammonia. The refluxing was complete when the solution pH was neutral. At that time, the heat was discontinued and the material, the pressure sensitive adhesive composition, was allowed to cool to less than 50°C.

Example 7 - In Situ Capping / 0.75% Acrylate capping by weight solids of PSA

In this example, the pressure sensitive adhesive composition of the present invention was prepared similar to the description above in Example 6, but containing a
higher level of silicon-containing capping agent. 273.74 g of Resin-1, 160.79 g of Polymer-1, 162.77 g of xylene, and 2.7 g of CA-2 were used to prepare the composition.

Example 8 - In Situ Capping / 1.0% Acrylate capping by weight solids of PSA
[00108] In this example, the pressure sensitive adhesive composition of the present invention was prepared similar to the description above in Example 6, but containing a higher level of silicon-containing capping agent. 273.05 g of Resin-1, 160.38 g of Polymer-1, 162.97 g of xylene, and 3.6 g of CA-2 were used to prepare the composition.

Example 9 - In Situ Capping / 2.5% Acrylate capping by weight solids of PSA
[00109] In this example, the pressure sensitive adhesive composition of the present invention was prepared similar to the description above in Example 6, but containing a higher level of silicon-containing capping agent. 274.6 g of Resin-1, 161.29 g of Polymer-1, 167.62 g of xylene, and 9.19 g of CA-2 were used to prepare the composition.

Example 10 - In Situ Capping / 5.0% Acrylate capping by weight solids of PSA
[00110] In this example, the pressure sensitive adhesive composition of the present invention was prepared similar to the description above in Example 6, but containing a higher level of silicon-containing capping agent. 262.01 g of Resin-1, 153.9 g of Polymer-1, 166.09 g of xylene, and 18.0 g of CA-2 were used to prepare the composition.

Example 11 - In Situ Capping / 1.0% Acrylate capping by weight solids of PSA
[00111] In this example, the pressure sensitive adhesive composition of the present invention was prepared similar to the description above in Example 6, but containing a higher level of silicon-containing capping agent. 273.05 g of Resin-1, 160.38 g of Polymer-1, 162.97 g of xylene, and 3.6 g of CA-3 were used to prepare the composition.

Example 12 - In Situ Capping / 2.5% Acrylate capping by weight solids of PSA
[00112] In this example, the pressure sensitive adhesive composition of the present invention was prepared similar to the description above in Example 6, but containing a higher level of silicon-containing capping agent. 268.95 g of Resin-1, 157.95 g of Polymer-1, 164.14 g of xylene, and 9.0 g of CA-3 were used to prepare the composition.

Example 13 - In Situ Capping / 5.0% Acrylate capping by weight solids of PSA
[00113] In this example, the pressure sensitive adhesive composition of the present invention was prepared similar to the description above in Example 6, but containing a
higher level of silicon-containing capping agent. 262.01 g of Resin-1, 153.9 g of Polymer-1, 166.09 g of xylene, and 18.0 g of CA-3 were used to prepare the composition.

[00114] For the above-referenced Examples;
[00115] the silicon-containing capping agent, CA-I, is 3-methacryloxypropyltrimethoxysilane commercially available from Gelest,
[00116] the silicon-containing capping agent, CA-2, is 3-methacryloxypropyltrimethoxysilane commercially available from Dow Corning Corporation under the tradename Z-6030, and
[00117] the silicon-containing capping agent, CA-3, is 3-methacryloxypropyltrimethoxysilane commercially available from Gelest.

[00118] Certain physical properties of the Examples (Control Example 1 - Example 13) are known and were measured according to the following Test Procedures. The physical properties are summarized below in Table 1.

NVC Test Procedure:
[00119] The non-volatile contents were determined by placing 2-4 grams (A) of the particular Example in an aluminum foil dish and heating the sample for 1 hour at 150°C in an air-circulating oven. The heated sample was then cooled to room temperature and reweighed to determine the weight of the nonvolatile material (B). The NVC, in percent, is equal to 100*B/A.

Viscosity Test Procedure:
[00120] The viscosity of the particular Example was determined at 25°C with a Brookfield® Viscometer Model RVT using spindle #5 at 12 rpm.

180 Degree Peel Adhesion Test Procedure:
[00121] Samples were prepared as follows: The particular Example was cast directly on 2.0 mil thick polyester sheets with the appropriate casting bar to afford a final adhesive thickness of 1.0 mil. Once cast, the sample was dried in an air-circulating oven at 60°C for 5 minutes. After cooling, the samples were cut into 1 inch wide strips. The strips were then applied to a stainless steel panel by rolling with 2 passes with a 4.5# steel roller. After equilibrating for 20 minutes on the stainless steel panel, the samples were then tested for 180 Degree Peel Adhesion at a rate of 12 inches per minute. Testing for
180 Degree Peel Adhesion is further understood by those skilled in the art with particular reference to ASTM D3330 and/or PSTC (Pressure Sensitive Tape Council)-1, which are typical standards for the 180 Degree Peel Adhesion.

<table>
<thead>
<tr>
<th>Example</th>
<th>Resulting Non-Volatile Content (NVC) % (i.e., weight % solids)</th>
<th>Viscosity (cps)</th>
<th>180 Degree Peel Adhesion (N/10mm)</th>
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Table 1

Using Control Examples 1 and 2 and also Examples 1-13 of the present invention, exemplary transdermal drug delivery systems were formed using niacinamide and ketoconazole as active agents. The niacinamide was loaded into the Control Examples and into the particular Examples of the invention at levels of 2% (Figures 1 and 2), 5% (Figures 3 and 4), and 10% (Figures 5 and 6). As noted above, Figures 1, 3, and 5 involve post capping of the capping agent and Figures 2, 4, and 6 involve in situ
capping of the capping agent. The ketoconazole was loaded into the Control Examples and into Examples 3 and 4 of the invention at levels of 2% (Figure 7), 5% (Figure 8), and 10% (Figure 9). As noted above, Figures 7-9 all involve post capping of the capping agent. Loading of the respective active agent is based on the total weight of the system.

More specifically, to test the release rate, samples were prepared by thoroughly mixing the respective active agent into the particular Example prior to casting and drying as generally described above under the ISO Degree Peel Adhesion Test Procedure. The release rate testing was performed using Franz static diffusion cells with the receptor fluid being specific for each drug. For niacinamide, the receptor fluid was 0.9% saline, and for ketoconazole, the receptor fluid was 40% PEG. Such release rate testing using Franz static diffusion cells is known in the art. Sampling time periods were from 1 to 24 hours, more specifically 1, 2, 3, 4, 6, 8 and 24 hours, with full receptor fluid replacement. These time periods are represented on the X-axis in Figures 1-9 as Time\textsuperscript{6}, i.e., the square root of the time. Analysis on the receptor fluid was conducted using a UV spectrophotometer at a wavelength specific for each active agent. For niacinamide, the specific wavelength was 261 nm and for ketoconazole, the specific wavelength was 269 nm.

As can be easily deduced from Figures 1-9, the addition of acrylate functionality via the silicon-containing capping agent increases the release rates for the active agents at all loading levels of the active agent (2, 5, and 10%) versus Control Examples 1 and 2 including the same loading levels of the active agents.

The invention has been described in an illustrative manner, and it is to be understood that the terminology which has been used is intended to be in the nature of words of description rather than of limitation. Obviously, many modifications and variations of the present invention are possible in light of the above teachings, and the invention may be practiced otherwise than as specifically described.
CLAIMS

What is claimed is:

1. A transdermal drug delivery system comprising:
   I. an active agent for controlled transdermal delivery to a substrate; and
   II. a pressure sensitive adhesive composition for maintaining contact with the substrate, said composition comprising the reaction product of:
      A. a pressure sensitive adhesive comprising the reaction product of:
         (i) a silicone resin, and
         (ii) a silicone polymer; and
      B. a silicon-containing capping agent comprising acrylate or methacrylate functionality.


3. A system as set forth in claim 1 wherein said pressure sensitive adhesive comprises a concentration of silicon bonded hydroxyl groups and said silicon-containing capping agent is further defined as an endblocking agent that reacts with said concentration of silicon bonded hydroxyl groups to cap said pressure sensitive adhesive.

4. A system as set forth in claim 3 wherein said endblocking agent is of the general formula (XYR₂Si)₂D wherein:
X is a monovalent radical of the general formula AE- where E is -O- or -NH- and
A is an acryl group or a methacryl group,

Y is a divalent alkylene radical having from 1 to 6 carbon atoms,

R is a methyl or a phenyl radical, and

D is a divalent or a trivalent organic hydrolyzable radical.

5. A system as set forth in claim 4 wherein D is -O- or -NH-.

6. A system as set forth in claim 4 wherein said endblocking agent is selected from the group of Bis(3-methacryloxypropyl)tetramethyldisilazane, Bis(3-acryloxypropyl)tetramethyldisilazane, Bis(3-methacryloxypropyl)tetramethyldisiloxane, Bis(3-acryloxypropyl)tetramethyldisiloxane, and combinations thereof.

7. A system as set forth in claim 3 wherein said endblocking agent is of the general formula XYR'bSiZ_{3-b} wherein;

X is a monovalent radical of the general formula AE- where E is -O- or -NH- and
A is an acryl group or a methacryl group,

Y is a divalent alkylene radical having from 1 to 6 carbon atoms,

R' is a methyl or a phenyl radical,

Z is a monovalent hydrolyzable organic radical or a halogen, and

b is 0, 1, or 2.

8. A system as set forth in claim 7 wherein said monovalent hydrolyzable organic radical is of the general formula R"O- where R" is an alkylene radical.

9. A hybrid composition as set forth in claim 7 wherein said endblocking agent is selected from the group of 3-methacryloxypropyl(dimethylchlorosilane, 3-
methacryloxypropylmethyldiethoxysilane, 3-methacryloxypropyltriethoxysilane, 3-methacryloxypropyldimethylsilazane, 3-methacryloxypropyldimethylchlorosilane, 3-acryloxypropylmethyldimethoxysilane, 3-acryloxypropylmethyldimethyldiethoxysilane, 3-acryloxypropylmethyldiethoxysilane, 3-acryloxypropyltriethoxysilane, 3-acryloxypropyltrisopropoxysilane, 3-acryloxypropyltrimethoxysilane, 3-acryloxypropyltrimethoxysilane, 3-acryloxypropyltrimethyldiethoxysilane, 3-acryloxypropyltriethoxysilane, 3-acryloxypropyltrimethyldiethoxysilane, 3-acryloxypropyltrimethyldiethoxysilane, and combinations thereof.

10. A system as set forth in claim 1 wherein said silicone resin comprises a copolymer comprising triorganosiloxoy units of the formula $R^3SiOi_2$ and tetrafunctional siloxy units of the formula $SiO_{4/2}$ in a ratio of about 0.6 to 0.9 triorganosiloxoy units for each tetrafunctional siloxy unit, wherein each $R^3$ independently denotes a monovalent hydrocarbon radical having from 1 to 6 carbon atoms; and said silicone polymer comprises at least one polydiorganosiloxane comprising AR$^3SiO$ units terminated with endblocking TR$^3ASiO_{1/2}$ units, wherein the polydiorganosiloxane has a viscosity of from about 100 centipoise to about 30,000,000
centipoise at 25°C, each A radical is independently selected from R³ or halohydrocarbon radicals having from 1 to 6 carbon atoms, each T radical is independently selected from the group consisting of R³, OH, H or OR⁴, and each R⁴ is independently an alkyl radical having from 1 to 4 carbon atoms.

11. A system as set forth in claim 10 wherein said silicone resin reacts in an amount of from 40 to 70 parts by weight to form said pressure sensitive adhesive, and said silicone polymer reacts in an amount of from 30 to 60 parts by weight to form said pressure sensitive adhesive, both based on 100 parts by weight of said pressure sensitive adhesive.

12. A system as set forth in claim 1 wherein said pressure sensitive adhesive is present in said composition in an amount of from 85.0 to 99.9 parts by weight based on weight % solids of said pressure sensitive adhesive, and said silicon-containing capping agent is present in said composition in an amount of from 0.1 to 15 parts by weight based on weight % solids of said pressure sensitive adhesive.

13. A system as set forth in claim 1 wherein said pressure sensitive adhesive is present in said composition in an amount of from 90.0 to 99.25 parts by weight based on weight % solids of said pressure sensitive adhesive, and said silicon-containing capping agent is present in said composition in an amount of from 0.75 to 10 parts by weight based on weight % solids of said pressure sensitive adhesive.

14. A system as set forth in claim 1 wherein said pressure sensitive adhesive comprises a catalytic amount of a condensation catalyst.
15. A system as set forth in claim 1 wherein said active agent is selected from the group of cardioactive medications, androgenic steroids, estrogens, hormones, external analgesics, progestational agents, drugs having an action on the central nervous system, nutritional agents, anti-inflammatory agents, antihistamines, respiratory agents, sympathomimetics, miotics, cholinergic agonists, antimuscarinic or muscarinic cholinergic blocking agents, mydriatics, psychicenergizers, anti-infectives, dermatological agents, humoral agents, antispasmodics, antidepressant drugs, anti-diabetic, anorectic drugs, anti-allergenics, tranquilizers, antipsychotics, decongestants, antipyretics, antimigraine agents, drugs for treating nausea and vomiting, anti-malarials, anti-ulcerative agents, peptides, drugs for Parkinson's disease, drugs for spasticity, drugs for acute muscle spasms, anti-estrogen, anti-hormone agents, therapeutic agents, and combinations thereof.

16. A system as set forth in claim 1 wherein said active agent is disposed in said pressure sensitive adhesive composition for the controlled transdermal delivery to the substrate.

17. A system as set forth in claim 1 wherein said active agent and said pressure sensitive adhesive composition coexist in said system in discrete layers.

18. A system as set forth in claim 1 further comprising:

- a backing layer for supporting said pressure sensitive adhesive composition;

and/or

- a release liner for protecting said pressure sensitive adhesive composition and/or said active agent prior to the controlled transdermal delivery to a substrate.
19. A system as set forth in claim 1 selected from the group of patches, films, multi-layer dressings, reservoir systems, and combinations thereof.

20. A system as set forth in claim 1 wherein said composition comprises a concentration of silicon bonded hydroxyl groups of from 5,000 to 15,000 ppm once said silicon-containing capping agent reacts with said pressure sensitive adhesive.

21. A system as set forth in claim 1 wherein said composition further comprises the reaction product of a second silicon-containing capping agent that is free of acrylate and methacrylate functionality.

22. A system as set forth in claim 21 wherein said second silicon-containing capping agent is capable of generating an endblocking triorganosilyl unit.
Drug Release Rates (Post Capping Reactions):
2% Niacinamide Loading, 0.9% Saline Receptor Fluid

- Control 1
- Control 2
- 0.5% Acryl-capping - Example 1
- 0.75% Acryl-capping - Example 2
- 1% Acryl-capping - Example 3
- 2.5% Acryl-capping - Example 4
- 5% Acryl-capping - Example 5

![Graph showing drug release rates](image-url)
Drug Release Rates (In Situ Capping Reactions):
2% Niacinamide Loading, 0.9% Saline Receptor Fluid

Figure 2
Drug Release Rates (In Situ Capped Reactions):
5% Niacinamide Loading, 0.9% Saline Receptor Fluid

Figure 4
Drug Release Rates (In Situ Capping Reactions):
10% Niacinamide Loading, 0.9% Saline Receptor Fluid

Figure 6
**Drug Release Rates (Post Capping Reactions):**
10% Ketoconazole Loading, 40% PEG Receptor Fluid

- Control 1
- Control 2
- 1% Acryl-capping - Example 3
- 2.5% Acryl-capping - Example 4

![Graph showing drug release rates over time with key data points and legend.](image-url)

**Figure 9**