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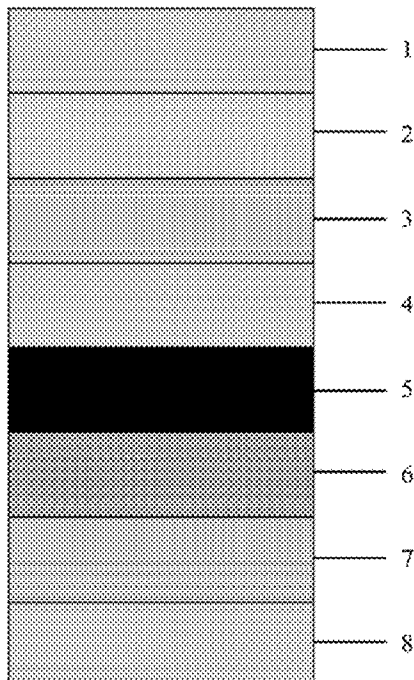
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ABSTRACT

A flexible, multilayer packaging film suitable for packaging an article for collecting or administering a physiologically active substance such as transdermal drug delivery patches, oral dissolvable thin strips, and disposable, microfluidic test cassettes having:

- (a) an article contact layer having at least 90 wt. % of a norbornene ethylene copolymer or derivative thereof and a glass transition temperature of from 65 to 110° C.;
- (b) a polyolefin bulk layer;
- (c) a first intermediate adhesive layer;
- (d) an oxygen barrier layer having an oxygen transmission rate of less than less than 0.01 cm³/100 inches²/24 hours at 1 atmosphere and 23° C.;
- (e) a second intermediate adhesive layer; and
- (f) an exterior protective layer comprising a polymer selected from the group consisting of amorphous polyester, polyamide, polyolefin, nylon, polypropylene, or copolymers, blends or derivatives thereof;

wherein said multilayer film has the following properties: a WVTR of less than 0.01 g/100 inches² per 24 hours at Room Temperature (RT) (23° C.) and 1 atmosphere; and a thickness of 10 mil or less.



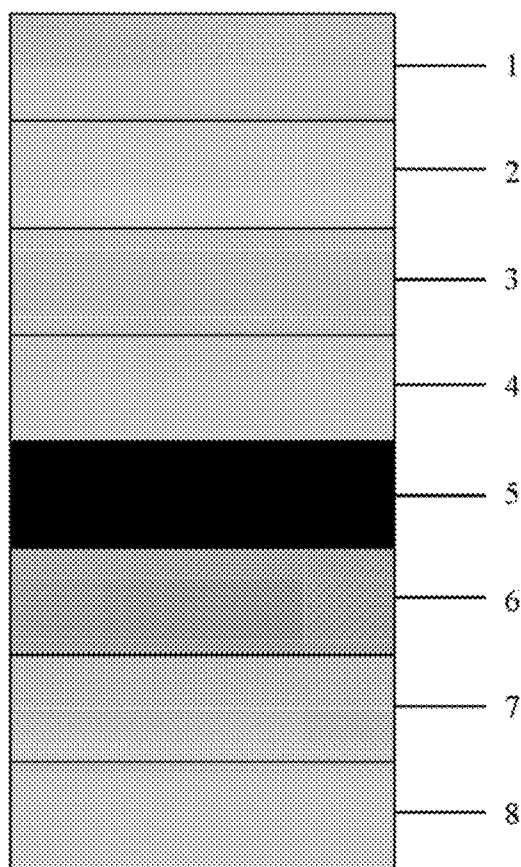


Fig 1

ANTI-SCALPING TRANSDERMAL PATCH PACKAGING FILM

BACKGROUND

[0001] 1. Technical Field

[0002] The present application relates generally to packaging suitable for packaging an article for collecting or administering a physiologically active substance such as transdermal drug delivery patches.

[0003] 2. Background Information

[0004] Pharmaceuticals such as the drugs fentanyl and nicotine are often administered through the use of transdermal patches which are applied to a patient's skin to permit drug delivery over time by absorption. Prior to application of a drug containing patch, the patch is packaged in a pouch which is designed to be opened to permit access to the patch by the patient or caregiver for application to a patient's skin. Suitable packaging for transdermal patches should contain the patch and its drug within the package while protecting the patch from contamination and deleterious effects from the external environment. Thus, articles such as a pouch may hold a transdermal patch to protect the patch and its drug contents from contact or exposure to unwanted materials such as microbes, insects, air, moisture, sunlight, etc. The container is typically sealed e.g. by a heat seal to provide a hermetic barrier.

[0005] The materials used in constructing transdermal patch packaging and especially the patch contact package interior surface layer should resist migration of chemicals between the patch and the package materials. Such migration of the drug or patch components from the patch to the package structure is referred to as "scalping". A common material employed for transdermal patch package interior surface layers that prevents scalping is polyacrylonitrile which is often sold under the Barex® trademark by Ineos AG. While Barex® has superb anti-scalping properties it is very expensive, poor tear properties that make pouch opening difficult, and has limited availability which creates supply chain risk because of its manufacture on only a single production reactor. Other polymers used in transdermal patch packaging as a surface contact layer include polyester. Polyester suffers from the disadvantage of being less resistant to scalping of certain chemicals than desired and its tear properties are also less than desired. Accordingly, there is a need for a more cost efficient packaging material for containing articles for collecting or administering a physiologically active substance such as transdermal drug delivery patches.

BRIEF SUMMARY

[0006] A flexible, multilayer packaging film suitable for packaging an article for collecting or administering a physiologically active substance such as transdermal drug delivery patches, oral dissolvable thin strips, and disposable, microfluidic test cassettes is provided having:

[0007] (a) an article contact layer having at least 90 wt. % of a norbornene ethylene copolymer or derivative thereof and a glass transition temperature of from 65 to 110° C.;

[0008] (b) a polyolefin bulk layer;

[0009] (c) a first intermediate adhesive layer;

[0010] (d) an oxygen barrier layer having an oxygen transmission rate of less than less than 0.01 cm³/100 inches²/24 hours at 1 atmosphere and 23° C.;

[0011] (e) a second intermediate adhesive layer; and

[0012] (f) an exterior protective layer comprising a polymer selected from the group consisting of amorphous polyester, polyamide, polyolefin, nylon, polypropylene, or copolymers, blends or derivatives thereof;

[0013] wherein said multilayer film has the following properties:

a WVTR of less than 0.01 g/100 inches² per 24 hours at Room Temperature (RT) (23° C.) and 1 atmosphere; and a thickness of 10 mil or less.

BRIEF DESCRIPTION OF THE DRAWINGS

[0014] FIG. 1 is a schematic view illustrating different layers of a multilayer film in accordance with the present invention.

DETAILED DESCRIPTION

Definitions and Nomenclature

[0015] In discussing polymer blends, plastic films and packaging, various acronyms are used herein and they are listed below. Also, in referring to blends of polymers a colon (:) will be used to indicate that the components to the left and right of the colon are blended. In referring to film structure, a slash "/" will be used to indicate that components to the left and right of the slash are in different layers and the relative position of components in layers may be so indicated by use of the slash to indicate film layer boundaries. Acronyms and terms commonly employed herein include:

APET—amorphous polyester terephthalate

OPET—biaxially oriented polyester terephthalate

COC—a cyclic olefin copolymer such as ethylene norbornene copolymer

PE—Polyethylene (ethylene homopolymer and/or copolymer of a major portion of ethylene with one or more α -olefins)

LDPE—low density polyethylene

LLDPE—linear low density polyethylene

mLLDPE—metallocene catalyzed linear low density polyethylene

C₂—ethylene monomer

C₄—butene-1 monomer

C₆—hexene-1 monomer

C₈—octene-1 monomer

C₁₀—decene-1 monomer

C₂C₈—a substantially linear copolymer of ethylene and an α -olefin where "x" indicates the number of carbon atoms in the comonomer.

VA—Vinyl Acetate

[0016] EVA—Copolymer of ethylene with vinyl acetate

EVOH—A saponified or hydrolyzed copolymer of ethylene and vinyl acetate

EAA—Copolymer of ethylene with acrylic acid

EMA—ethylene methacrylic acid copolymer

ionomer—an ethylene-methacrylate acid copolymer whose acid groups have been neutralized partly or completely to form a salt, preferably a zinc or sodium salt

PVDC—Polyvinylidene chloride (also includes copolymers of vinylidene chloride, especially with vinyl chloride)

[0017] The term "nanocomposite" shall mean a mixture that includes a polymer, or copolymer having dispersed therein a plurality of individual platelets obtained from an exfoliated modified clay and having oxygen barrier properties.

[0018] The term “adhesive layer,” or “tie layer,” refers to a layer or material placed on one or more layers to promote the adhesion of that layer to another surface. Preferably, adhesive layers are positioned between two layers of a multilayer film to maintain the two layers in position relative to each other and prevent undesirable delamination. In some embodiments a peelable tie layer may be used which is designed to have either cohesive failure or delamination from one or both adjacent layers upon application of a suitable manual force to provide an opening feature for a package made from the film. Unless otherwise indicated, an adhesive layer can have any suitable composition that provides a desired level of adhesion with the one or more surfaces in contact with the adhesive layer material. Optionally, an adhesive layer placed between a first layer and a second layer in a multilayer film may comprise components of both the first layer and the second layer to promote simultaneous adhesion of the adhesive layer to both the first layer and the second layer to opposite sides of the adhesive layer.

[0019] As used herein, unless otherwise indicated, the phrases “seal layer,” “sealing layer,” “heat seal layer,” and “sealant layer,” refer to a film layer, or layers, involved in the sealing of the film: to itself; to another film layer of the same film or another film; and/or to another article which is not a film e.g. a tray. In general, the sealant layer is a surface layer i.e. an exterior or an interior layer of any suitable thickness, that provides for the sealing of the film to itself or another layer. With respect to packages having only fin-type seals, as opposed to lap-type seals, the phrase “sealant layer” generally refers to the interior surface film layer of a package. The inside layer frequently can also serve as an article contact layer in the packaging of articles.

[0020] “Polyolefin” is used herein broadly to include polymers such as polyethylene, ethylene- α olefin copolymers (EAO), polypropylene, polybutene, ethylene copolymers having a majority amount by weight of ethylene polymerized with a lesser amount of a comonomer such as vinyl acetate, and other polymeric resins falling in the “olefin” family classification. Polyolefins may be made by a variety of processes well known in the art including batch and continuous processes using single, staged or sequential reactors, slurry, solution and fluidized bed processes and one or more catalysts including for example, heterogeneous and homogeneous systems and Ziegler, Phillips, metallocene, single site and constrained geometry catalysts to produce polymers having different combinations of properties. Such polymers may be highly branched or substantially linear and the branching, dispersity and average molecular weight and may vary depending upon the parameters and processes chosen for their manufacture in accordance with the teachings of the polymer arts.

[0021] “Polyethylene” is the name for a polymer whose basic structure is characterized by the chain $-(CH_2-CH_2-)_n-$. Polyethylene homopolymer is generally described as being a solid which has a partially amorphous phase and partially crystalline phase with a density of between 0.915 to 0.970 g/cm³. The relative crystallinity of polyethylene is known to affect its physical properties. The amorphous phase imparts flexibility and high impact strength while the crystalline phase imparts a high softening temperature and rigidity.

[0022] Unsubstituted polyethylene is generally referred to as high density homopolymer and has a crystallinity of 70 to 90 percent with a density between about 0.96 to 0.97 g/cm³. Most commercially utilized polyethylenes are not unsubsti-

tuted homopolymer but instead have C₂-C₈ alkyl groups attached to the basic chain. These substituted polyethylenes are also known as branched chain polyethylenes. Also, commercially available polyethylenes frequently include other substituent groups produced by copolymerization. Branching with alkyl groups generally reduces crystallinity, density and melting point. The density of polyethylene is recognized as being closely connected to the crystallinity. The physical properties of commercially available polyethylenes are also affected by average molecular weight and molecular weight distribution, branching length and type of substituents.

[0023] People skilled in the art generally refer to several broad categories of polymers and copolymers as “polyethylene.” Placement of a particular polymer into one of these categories of “polyethylene” is frequently based upon the density of the “polyethylene” and often by additional reference to the process by which it was made since the process often determines the degree of branching, crystallinity and density. In general, the nomenclature used is nonspecific to a compound but refers instead to a range of compositions. This range often includes both homopolymers and copolymers.

[0024] For example, “high density” polyethylene (HDPE) is ordinarily used in the art to refer to both (a) homopolymers of densities between about 0.960 to 0.970 g/cm³ and (b) copolymers of ethylene and an α -olefin (usually 1-butene or 1-hexene) which have densities between 0.940 and 0.958 g/cm³. HDPE includes polymers made with Ziegler or Phillips type catalysts and is also said to include high molecular weight “polyethylenes.” In contrast to HDPE, whose polymer chain has some branching, are “ultra high molecular weight polyethylenes” which are essentially unbranched specialty polymers having a much higher molecular weight than the high molecular weight HDPE.

[0025] Hereinafter, the term “polyethylene” will be used (unless indicated otherwise) to refer to ethylene homopolymers as well as copolymers of ethylene with α -olefins and the term will be used without regard to the presence or absence of substituent branch groups.

[0026] Another broad grouping of polyethylene is “high pressure, low density polyethylene” (LDPE). LDPE is used to denominate branched homopolymers having densities between 0.915 and 0.930 g/cm³. LDPEs typically contain long branches off the main chain (often termed “backbone”) with alkyl substituents of 2 to 8 carbon atoms.

[0027] Linear Low Density Polyethylene (LLDPE) are copolymers of ethylene with α -olefins having densities from 0.915 to 0.940 g/cm³. The α -olefin utilized is usually 1-butene, 1-hexene, or 1-octene and Ziegler-type catalysts are usually employed (although Phillips catalysts are also used to produce LLDPE having densities at the higher end of the range, and metallocene and other types of catalysts are also employed to produce other well known variations of LLDPEs). An LLDPE produced with a metallocene or constrained geometry catalyst is often referred to as “mLLDPE”.

[0028] Ethylene α -olefin copolymers are copolymers having an ethylene as a major component copolymerized with one or more α olefins such as octene-1, hexene-, or butene-1 as a minor component. EAOs include polymers known as LLDPE, VLDPE, ULDPE, and plastomers and may be made using a variety of processes and catalysts including metallocene, single-site and constrained geometry catalysts as well as Ziegler-Natta and Phillips catalysts.

[0029] Very Low Density Polyethylene (VLDPE) which is also called “Ultra Low Density Polyethylene” (ULDPE)

comprise copolymers of ethylene with α -olefins, usually 1-butene, 1-hexene or 1-octene and are recognized by those skilled in the art as having a high degree of linearity of structure with short branching rather than the long side branches characteristic of LDPE. However, VLDPEs have lower densities than LLDPEs. The densities of VLDPEs are recognized by those skilled in the art to range between 0.860 and 0.915 g/cm³. Sometimes VLDPEs having a density less than 0.900 g/cm³ are referred to as "plastomers".

[0030] Polyethylenes may be used alone, in blends and/or with copolymers in both monolayer and multilayer films for packaging applications.

[0031] As used herein, the term "modified" refers to a chemical derivative e.g. one having any form of anhydride functionality, such as anhydride of maleic acid, crotonic acid, citraconic acid, itaconic acid, fumaric acid, etc., whether grafted onto a polymer, copolymerized with a polymer, or otherwise functionally associated with one or more polymers, and is also inclusive of derivatives of such functionalities, such as acids, esters, and metal salts derived therefrom. Another example of a common modification is acrylate modified polyolefins.

[0032] As used herein, terms identifying polymers, such as e.g. "polyamide" or "polypropylene," are inclusive of not only polymers comprising repeating units derived from monomers known to polymerize to form a polymer of the named type, but are also inclusive of comonomers, as well as both unmodified and modified polymers made by e.g. derivatization of a polymer after its polymerization to add functional groups or moieties along the polymeric chain. Furthermore, terms identifying polymers are also inclusive of "blends" of such polymers. Thus, the terms "polyamide polymer" and "nylon polymer" may refer to a polyamide-containing homopolymer, a polyamide-containing copolymer or mixtures thereof.

[0033] The term "polyamide" means a high molecular weight polymer having amide linkages ($-\text{CONH}-$), which occur along the molecular chain, and includes "nylon" resins which are well known polymers having a multitude of uses including utility as packaging films, bags, and pouches. See, e.g. *Modern Plastics Encyclopedia*, 88 Vol. 64, No. 10A, pp 34-37 and 554-555 (McGraw-Hill, Inc., 1987) which is hereby incorporated by reference. Polyamides are preferably selected from nylon compounds approved for use in producing articles intended for use in processing, handling, and packaging food or drugs.

[0034] The term "nylon" as used herein it refers more specifically to synthetic polyamides, either aliphatic or aromatic, either in crystalline, semi-crystalline, or amorphous form characterized by the presence of the amide group $-\text{CONH}-$. It is intended to refer to both polyamides and co-polyamides.

[0035] Thus the terms "polyamide" or "nylon" encompass both polymers comprising repeating units derived from monomers, such as caprolactam, which polymerize to form a polyamide, as well as copolymers derived from the copolymerization of caprolactam with a comonomer which when polymerized alone does not result in the formation of a polyamide. Preferably, polymers are selected from compositions approved as safe for producing articles intended for use in processing, handling and packaging of food or drugs, such as nylon resins approved by the U.S. Food and Drug Administration provided at 21 CFR .sectn. 177.1500 ("Nylon resins"), which is incorporated herein by reference. Examples of these nylon polymeric resins for use in food or drug packaging and

processing include: nylon 66, nylon 610, nylon 66/610, nylon 6/66, nylon 11, nylon 6, nylon 66T, nylon 612, nylon 12, nylon 6/12, nylon 6/69, nylon 46, nylon 6-3-T, nylon MXD-6, nylon MXD1, nylon 12T and nylon 61/6T disclosed at 21 CFR .sectn. 177.1500. Examples of such polyamides include nylon homopolymers and copolymers such as those selected from the group consisting of nylon 4,6 (poly(tetramethylene adipamide)), nylon 6 (polycaprolactam), nylon 6,6 (poly(hexamethylene adipamide)), nylon 6,9 (poly(hexamethylene nonanediamide)), nylon 6,10 (poly(hexamethylene sebacamide)), nylon 6,12 (poly(hexamethylene dodecanediamide)), nylon 6/12 (poly(caprolactam-co-dodecanediamide)), nylon 6,6/6 (poly(hexamethylene adipamide-co-caprolactam)), nylon 66/610 (e.g., manufactured by the condensation of mixtures of nylon 66 salts and nylon 610 salts), nylon 6/69 resins (e.g., manufactured by the condensation of epsilon-caprolactam, hexamethylenediamine and azelaic acid), nylon 11 (polyundecanolactam), nylon 12 (polylauryllactam) and copolymers or mixtures thereof.

[0036] In use of the term "amorphous nylon copolymer," the term "amorphous" as used herein denotes an absence of a regular three-dimensional arrangement of molecules or sub-units of molecules extending over distances which are large relative to atomic dimensions. However, regularity of structure may exist on a local scale. See, "Amorphous Polymers," *Encyclopedia of Polymer Science and Engineering*, 2nd Ed., pp. 789-842 (J. Wiley & Sons, Inc. 1985). In particular, the term "amorphous nylon copolymer" refers to a material recognized by one skilled in the art of differential scanning calorimetry (DSC) as having no measurable melting point (less than 0.5 cal/g) or no heat of fusion as measured by DSC using ASTM 3417-83. The amorphous nylon copolymer may be manufactured by the condensation of hexamethylenediamine, terephthalic acid, and isophthalic acid according to known processes. Amorphous nylons also include those amorphous nylons prepared from condensation polymerization reactions of diamines with dicarboxylic acids. For example, an aliphatic diamine is combined with an aromatic dicarboxylic acid, or an aromatic diamine is combined with an aliphatic dicarboxylic acid to give suitable amorphous nylons.

[0037] As used herein, "EVOH" refers to ethylene vinyl alcohol copolymer. EVOH is otherwise known as saponified or hydrolyzed ethylene vinyl acetate copolymer, and refers to a vinyl alcohol copolymer having an ethylene comonomer. EVOH is prepared by the hydrolysis (or saponification) of an ethylene-vinyl acetate copolymer. The degree of hydrolysis is preferably from about 50 to 100 mole percent, more preferably, from about 85 to 100 mole percent, and most preferably at least 97%. It is well known that to be a highly effective oxygen barrier, the hydrolysis-saponification must be nearly complete, i.e. to the extent of at least 97%. EVOH is commercially available in resin form with various percentages of ethylene and there is a direct relationship between ethylene content and melting point. For example, EVOH having a melting point of about 175° C. or lower is characteristic of EVOH materials having an ethylene content of about 38 mole % or higher. EVOH having an ethylene content of 38 mole % has a melting point of about 175° C. With increasing ethylene content the melting point is lowered. Also, EVOH polymers having increasing mole percentages of ethylene have greater gas permeabilities. A melting point of about 158° C. corresponds to an ethylene content of 48 mole %. EVOH copolymers having lower or higher ethylene contents may also be

employed. It is expected that processability and orientation would be facilitated at higher contents, however, gas permeabilities, particularly with respect to oxygen, may become undesirably high for certain packaging applications which are sensitive to microbial growth in the presence of oxygen. Conversely lower contents may have lower gas permeabilities, but processability and orientation may be more difficult.

[0038] As used herein, the term “polyester” refers to synthetic homopolymers and copolymers having ester linkages between monomer units which may be formed by condensation polymerization methods. Polymers of this type are preferable aromatic polyesters and more preferable, homopolymers and copolymers of poly(ethylene terephthalate), poly(ethylene isophthalate), poly(butylene terephthalate), poly(ethylene naphthalate) and blends thereof. Suitable aromatic polyesters may have an intrinsic viscosity between 0.60 to 1.0, preferably between 0.60 to 0.80.

[0039] The terms “heat sealing layer” or “sealant layer” are used interchangeably to refer to a layer which is heat sealable i.e., capable of fusion bonding by conventional indirect heating means which generate sufficient heat on at least one film contact surface for conduction to the contiguous film contact surface and formation of a bond interface therebetween without loss of the film integrity. The bond interface between contiguous inner layers preferably has sufficient physical strength to withstand the packaging process and subsequent handling. Advantageously, the bond interface is preferably sufficiently thermally stable to prevent gas or liquid leakage therethrough when exposed to above or below ambient temperatures e.g. during one or more of the following: packaging operations, storage, handling, and transport. Heat seals may be designed to meet different conditions of expected use and various heat seal formulations are known in the art and may be employed with the present invention. Preferably the article contact or heat seal layer is heat sealable to itself, but may be sealable to other objects, films or layers e.g. to a tray when used as a lidding film, or to an outer layer in a lap seal or in certain tray overwrap embodiments.

[0040] Article Contact/Heat Sealing Layers

[0041] It is essential that the oxygen and water barrier film of the present invention have an article contact layer containing ethylene norbornene copolymer which is a cyclic olefin copolymer (COC). COCs are commercially available from Topas as an amorphous, transparent copolymer of ethylene with norbornene made by polymerization with a metallocene catalyst. These commercially available COCs reportedly have high transparency and gloss, excellent moisture barrier and aroma barrier properties, a variable glass transition point between 65 to 178° C., high stiffness, high strength, excellent biocompatibility and inertness and easy to exclude and thermoform. COCs have previously been used for pharmaceutical, medical and food packaging applications including use in coextruded cast films for blister packaging and may be blended with polyethylene. For the present invention, ethylene norbornene copolymers having a glass transition temperature (T_g) of 65-138° C. or an ethylene-norbornene comonomer content of 20-40 mole % ethylene and 30-60 mole % norbornene is required. These ethylene norbornene copolymers are believed to comprise essentially only polymeric units derived from ethylene and norbornene comonomers. Other reported properties for the ethylene norbornene copolymers used in the present invention include a density (Δ) of 1.02 g/cm³; a melt volume ratio (MVR) of 1.0-12.0 cm³/10 min. at 230° C., 2.16 kg load, and 1.0-2.0 at 190° C.,

2.16 kg load (ISO 1133); a melt index of 0.1 to 1.9 at 190° C., 2.16 kg load (reported as calculated from ISO 1133 MVR using a melt density of 0.92). Other properties of Topas cyclic olefin copolymer are described in a March 2006 brochure “Topas® Cyclic Olefin Copolymers” available from Topas Advanced Polymers on its website: http://www.topas.com/sites/default/files/files/topas_product-brochure_english.pdf which brochure is hereby incorporated by reference in its entirety. In the present invention the contact layer may also function as a heat sealing or heat sealable layer to facilitate formation of hermetically sealed packages. The article contact layer comprises at least 90 wt. % of ethylene norbornene COC, more preferably at least 95 wt. %, and most preferably 100 wt. %. It may be blended with up to 10 wt. %, preferably up to 5 wt. % and more preferably up to 2.5 wt. % of compatible polymers such as polyolefins e.g. polyethylene, LLDPE, EAO copolymers, LDPE, colorants, processing aids and the like. Use of these polymers and components in a blend with the COC may undesirable affect the essential anti-scalping properties of this layer and addition of amounts above 10 wt. % is unacceptable for most applications of the film for packaging drugs or drug articles such as transdermal patches e.g. nicotine patches or fentanyl patches.

[0042] The terms “heat sealing layer” or “sealant layer” are used interchangeably to refer to a layer which is heat sealable i.e., capable of fusion bonding by conventional indirect heating means which generate sufficient heat on at least one film contact surface for conduction to the contiguous film contact surface and formation of a bond interface therebetween without loss of the film integrity. The bond interface between contiguous inner layers preferably has sufficient physical strength to withstand the packaging process and subsequent handling. Advantageously, the bond interface is preferably sufficiently thermally stable to prevent gas or liquid leakage therethrough when exposed to above or below ambient temperatures e.g. during one or more of the following: packaging operations, storage, handling, and transport.

Barrier Layers

[0043] The barrier layer preferably functions both as a gas barrier layer, and as a moisture barrier layer, although these functions may be provided by separate layers. The gas barrier layer is preferably an oxygen barrier layer, and is preferably a core layer positioned between and protected by surface layers. For example, the oxygen barrier layer can be in contact with a first surface layer and an adhesive layer or may be sandwiched between two tie layers and/or two surface layers.

[0044] The oxygen barrier is preferably selected to provide an oxygen permeability sufficiently diminished to protect the packaged article from undesirable deterioration or oxidative processes. For example, a film may comprise an oxygen barrier having an oxygen permeability that is low enough to prevent oxidation of oxygen sensitive articles and substances to be packaged in the film e.g. oxygen sensitive articles such as transdermal patches e.g. nicotine or fentanyl patches or oxygen sensitive collection samples such as blood which may be collected e.g. in a microcassette device. Preferably a multilayer packaging film in accordance with the present invention will have an oxygen barrier of less than or equal to 10 cm³/100 inches²/24 hours at 1 atmosphere and 23° C., more preferably less than 0.016 cm³/m² per 24 hours at 1 atmosphere. To protect oxygen sensitive articles from deterioration from oxygen contact over time the films according to the present invention will have a preferred oxygen transmission

rate (O_2TR) of less than 1, preferably less than 0.1, more preferably less than 0.01, and most preferably less than 0.001 g/100 inches² at 24 hours at Room Temperature (RT) (~23° C.) and 1 atmosphere (<0.001 g/m² at 24 hours at Room Temperature (RT) (~23° C.)) and 1 atmosphere).

[0045] The water or moisture barrier is preferably selected to provide a moisture permeability sufficiently diminished to protect the packaged article from undesirable deterioration. For example, a film may comprise an water barrier having an moisture permeability that is low enough to prevent deleterious effects upon packaged articles such as transdermal drug patches or other moisture sensitive products. A preferred film according to the present invention will have a water or moisture transmission rate (WVTR) of less than 0.001 g/100 inches² per 24 hours at Room Temperature (RT) (23° C.) and 1 atmosphere.

[0046] The oxygen and moisture barrier layer can comprise any suitable material. An oxygen barrier layer can comprise EVOH, polyvinylidene chloride, polyamide, polyester, polyalkylene carbonate, polyacrylonitrile, nanocomposite, a metallized film such as aluminum vapor deposited on a polyolefin, etc., as known to those of skill in the art. Suitable moisture barrier layers include aluminum foil, PVDC, or polyolefins such as LDPE or LLDPE. It is desirable that the thickness of the barrier layer be selected to provide the desired combination of the performance properties sought e.g. with respect to oxygen permeability, and delamination resistance, and water barrier properties. Suitable thicknesses in multilayer films are less than 15%, e.g. from 3 to 13% of the total film thickness and preferably less than about 10% of the total thickness of the multilayer film. Greater thicknesses may be employed however oxygen barrier polymers tend to be relatively expensive and therefore it is expected that less costly resins will be used in other layers to impart desirable properties once a suitable thickness is used to achieve the desired gas barrier property for the film layer combination. For example, the thickness of a core oxygen barrier layer may advantageously be less than about 0.45 mil (10.16 microns) and greater than about 0.05 mil (1.27 microns), including 0.10, 0.20, 0.25, 0.30, 0.40, or 0.45 mil thick.

[0047] The oxygen barrier layer of a film may comprise aluminum foil, or EVOH, although oxygen barrier layers comprising polyvinylidene chloride-vinyl chloride copolymer (PVDC or VDC-VC) or vinylidene chloride-methylacrylate copolymer (VDC-MA) as well as blends thereof, can also be used. One suitable EVOH barrier material is a 44 mol % EVOH resin E151B sold by Eval Company of America, under the trade name Eval®LC-E151B. Another example of an EVOH that may be acceptable can be purchased from Nippon Gohsei under the trade name Soarnol® AT (44 mol % ethylene EVOH).

[0048] For packaging of oxygen sensitive articles such as drug patches, an oxygen (O_2) permeability of less than about 310 cm³/m² for a 24 hour period at 1 atmosphere, 0% relative humidity and 23° C., and preferably less than 75 cm³/m², more preferably less than 20 cm³/m². The thickness of the core layer may be varied and beneficially may be from about 0.05 to about 0.60 mils (1.3-15.2 microns).

[0049] A bulk layer may be provided to provide additional functionality such as stiffness or heat sealability or to improve machinability, cost, flexibility, barrier properties, etc. Preferred bulk layers comprise one or more polyolefins such as polyethylene, ethylene-alpha olefin copolymers (EAO), polypropylene, polybutene, ethylene copolymers having a

majority amount by weight of ethylene polymerized with a lesser amount of a comonomer such as vinyl acetate, and other polymeric resins falling in the "olefin" family classification. The bulk layer may be of any suitable thickness from 0.1 to 7 mils or may even be omitted for use in certain applications, but is preferably present to improve especially stiffness/flexibility properties and heat sealability.

[0050] Abuse-Resistant Outer Layer

[0051] Since it is seen by the user/consumer, in both the monolayer and multilayer embodiments of the invention the exterior surface of the film should enhance optical properties of the film and may preferably have high gloss. Also, it should withstand contact with sharp objects and provide abrasion resistance, and for these reasons it is often termed the abuse-resistant layer. This exterior abuse-resistant layer may or may not also be used as a heat sealable layer. As the exterior surface layer of the film, this layer most often is also the exterior layer of any package, bag, pouch or other container made from the inventive film, and is therefore subject to handling and abuse e.g. from equipment during packaging, and from rubbing against other packages and shipping containers and storage shelves during transport and storage. This contact causes abrasive forces, stresses and pressures which may abrade away the film causing defects to printing, diminished optical characteristics or even punctures or breaches in the integrity of the package. Therefore the exterior surface layer is typically made from materials chosen to be resistant to abrasive and puncture forces and other stresses and abuse which the packaging may encounter during use. The exterior surface layer should be easy to machine (i.e. be easy to feed through and be manipulated by machines e.g. for conveying, packaging, printing or as part of the film or bag manufacturing process). Suitable stiffness, flexibility, flex crack resistance, modulus, tensile strength, coefficient of friction, printability, and optical properties are also frequently designed into exterior layers by suitable choice of materials. This layer may also be chosen to have characteristics suitable for creating desired heat seals which may be heat resistance to burn through e.g. by impulse sealers or may be used as a heat sealing surface in certain package embodiments e.g. using overlap seals. The exterior layer may be tough to impart resistance to opening by children e.g. preventing the package from being opened by a child's bite. A preferred exterior child resistant layer comprise polyester film, preferably polyester terephthalate, preferably at least 0.9 mil in thickness. Suitable exterior surface layers may comprise: paper, oriented polyester, amorphous polyester, polyamide, polyolefin, cast or oriented nylon, polypropylene, or copolymers, blends or derivatives thereof. Oriented films of this or any other layer may be either uni-axially or bi-axially oriented.

[0052] The exterior layer thickness is typically 0.5 to 2.0 mils. Thinner layers may be less effective for abuse resistance, however thicker layers, though more expensive, may advantageously be used to produce films having unique highly desirable puncture resistance and/or abuse resistance properties.

Intermediate Layers

[0053] An intermediate layer is any layer between the exterior layer and the interior layer and may include oxygen barrier layers, tie layers or layers having functional attributes useful for the film structure or its intended uses. Intermediate layers may be used to improve, impart or otherwise modify a multitude of characteristics: e.g. printability for trap printed

structures, machinability, tensile properties, flexibility, stiffness, modulus, designed delamination, easy opening features, tear properties, strength, elongation, optical, moisture barrier, oxygen or other gas barrier, radiation selection or barrier e.g. to ultraviolet wavelengths, etc. Suitable intermediate layers may include: adhesives, adhesive polymers, paper, oriented polyester, amorphous polyester, polyamide, polyolefin, nylon, polypropylene, or copolymers, blends or derivatives thereof. Suitable polyolefins may include: polyethylene, ethylene-alpha olefin copolymers (EAO), polypropylene, polybutene, ethylene copolymers having a majority amount by weight of ethylene polymerized with a lesser amount of a comonomer such as vinyl acetate, and other polymeric resins falling in the "olefin" family classification, LDPE, HDPE, LLDPE, EAO, ionomer, EMA, EAA, modified polyolefins e.g. anhydride grafted ethylene polymers, etc.

Tie Layers

[0054] In addition to the exterior layer, the interior layer, and intermediate layer such as a barrier layer, a multilayer packaging film can further comprise one or more adhesive layers, also known in the art as "tie layers," which can be selected to promote the adherence of adjacent layers to one another in a multilayer film and prevent undesirable delamination. A multifunctional layer is preferably formulated to aid in the adherence of one layer to another layer without the need of using separate adhesives by virtue of the compatibility of the materials in that layer to the first and second layers. In some embodiments, adhesive layers comprise materials found in both the first and second layers. The adhesive layer may suitably be less than 10% and preferably between 2% and 10% of the overall thickness of the multilayer film. Adhesive resins are often more expensive than other polymers so the tie layer thickness is usually kept to a minimum consistent with the desired effect. In one embodiment, a multilayer film comprises a multilayer structure comprising a first adhesive layer positioned between and in direct contact with the exterior layer and a core oxygen barrier layer; and preferably and optionally has a second tie layer between and in direct contact with the same core oxygen barrier layer and the interior layer to produce a five layer film. Adhesive layers may include modified e.g. anhydride modified polymers e.g. polyolefins such as polyethylenes or ethylene copolymers such as EVA and may also be primers or specialty adhesive resins.

[0055] Multilayer films can comprise any suitable number of tie or adhesive layers of any suitable composition. Various adhesive layers are formulated and positioned to provide a desired level of adhesive between specific layers of the film according to the composition of the layers contacted by the tie layers.

[0056] For example adhesive layers in contact with a layer comprising a polyester, such as PET, preferably comprise a suitable blend of polyolefins with other adhesive polymers. One preferred component of an adhesive layer in contact with a PET polyester layer is EMAC SP 1330 (which reportedly has: a density of 0.948 g/cm³; melt index of 2.0 g/10 min.; a melting point of 93.degree. C.; is at softening point of 49° C.; and a methylacrylate (MA) content of 22%).

[0057] The interior, exterior, intermediate or tie layers may be formed of any suitable thermoplastic materials, for example, polyamides, polystyrenes, styrenic copolymers e.g. styrene-butadiene copolymer, polyolefins, and in particular members of the polyethylene family such as LLDPE,

VLDPE, HDPE, LDPE, ethylene vinyl ester copolymer or ethylene alkyl acrylate copolymer, polypropylenes, ethylene-propylene copolymers, ionomers, polybutylenes, alpha-olefin polymers, polyesters, polyurethanes, polyacrylamides, anhydride-modified polymers, acrylate-modified polymers, polylactic acid polymers, or various blends of two or more of these materials.

[0058] In another embodiment, the exterior, interior and/or one or more intermediate layers can comprise or consist essentially of a nylon blend composition. Preferably, the nylon blend composition comprises at least an amorphous nylon such as nylon 6I/6T copolymer, in combination with at least one semi-crystalline nylon homopolymer or copolymer such as nylon 6/12, 6/69, 6/66, MXD6, 6, 11, or 12.

[0059] In another embodiment of the invention one or more of the exterior, interior and/or one or more intermediate layers comprises at least one polyester polymer. Preferred polyester polymers comprise aromatic polyesters and more preferably, are homopolymers or copolymers of poly(ethylene terephthalate) (PET), poly(ethylene naphthalate) and blends thereof. Suitable polyesters may have an intrinsic viscosity of about 0.60 to about 1.2, preferably between 0.60 to 0.80. The polyester may be an aliphatic polyester resin, but is preferably an aromatic polyester resin. For example, polyester materials can be derived from dicarboxylic acid components, including terephthalic acid and isophthalic acid as preferred examples, and also dimers of unsaturated aliphatic acids. Examples of a diol component as another component for synthesizing the polyester may include: polyalkylene glycols, such as ethylene glycol, propylene glycol, tetramethylene glycol, neopentyl glycol, hexamethylene glycol, diethylene glycol, polyethylene glycol and polytetra methylene oxide glycol; 1,4-cyclohexane-dimethanol, and 2-alkyl-1,3-propanediol. More specifically, examples of dicarboxylic acids constituting the polyester resin may include: terephthalic acid, isophthalic acid, phthalic acid, 5-t-butylisophthalic acid, naphthalenedicarboxylic acid, diphenyl ether dicarboxylic acid, cyclohexane-dicarboxylic acid, adipic acid, oxalic acid, malonic acid, succinic acid, azelaic acid, sebacic acid, and dimer acids comprising dimers of unsaturated fatty acids. These acids may be used singly or in combination of two or more species. Examples of diols constituting the polyester resin may include: ethylene glycol, propylene glycol, tetramethylene glycol, neopentyl glycol, hexamethylene glycol, diethylene glycol, polyalkylene glycol, 1,4-cyclohexane-dimethanol, 1,4-butanediol, and 2-alkyl-1,3-propane diol. These diols may be used singly or in combination of two or more species.

[0060] Polyester compositions that comprise an aromatic polyester resin comprising an aromatic dicarboxylic acid component can be preferred in some aspects, including, e.g., polyesters between terephthalic acid (as a dicarboxylic acid) and diols having at most 10 carbon atoms, such as polyethylene terephthalate and polybutylene terephthalate. Particularly preferred examples thereof may include: copolyesters obtained by replacing a portion, preferably at most 30 mol %, more preferably at most 15 mol %, of the terephthalic acid with another dicarboxylic acid, such as isophthalic acid; copolyesters obtained by replacing a portion of the diol component such as ethylene glycol with another diol, such as 1,4-cyclohexane-dimethanol (e.g., "Voridian 9921", made by Voridian division of Eastman Chemical Co.); and polyester-polyether copolymers comprising the polyester as a predominant component (e.g., polyester-ether between a dicarboxylic acid component principally comprising terephthalic acid

or/and its ester derivative and a diol component principally comprising tetramethylene glycol and tetramethylene oxide glycol, preferably containing the polytetra methylene oxide glycol residue in a proportion of 10-15 wt. %). It is also possible to use two or more different polyester resins in mixture. Examples of preferred polyesters are available under the trademarks Voridian 9663, Voridian 9921 and EASTAR® Copolyester 6763, all from Eastman Chemical Company, Kingsport, Tenn., U.S.A.

Optional Additives to Layers

[0061] Various additives may be included in the polymers utilized in one or more of the exterior, interior and intermediate or tie layers of food packaging comprising the same. For example, a layer may be coated with an anti-block powder. Also, conventional anti-oxidants, antiblock additives, polymeric plasticizers, acid, moisture or gas (such as oxygen) scavengers, slip agents, colorants, dyes, pigments, organoleptic agents may be added to one or more film layers of the film or it may be free from such added ingredients. If the exterior layer is corona treated, preferably no slip agent will be used, but it will contain or be coated with an anti-block powder or agent such as silica or starch. Processing aides are typically used in amounts less than 10%, less than 7% and preferably less than 5% of the layer weight. A preferred processing aid for use in the outer layer of the film includes one or more of fluoroelastomers, stearamides, erucamides, and silicates.

[0062] Preferred films may also provide a beneficial combination of one or more or all of the properties including low haze, high gloss, good machinability, good mechanical strength and good barrier properties including high barriers to oxygen and water permeability. Suitable barrier properties may have values of WVTR less than or equal to 0.03 g/100 in²/24 hours at 1 atmosphere and RT, and/or O₂TR values of less than or equal to 10 cm³/100 in²/24 hours at 1 atmosphere and RT. Preferred barrier property values are WVTR < 0.001 g/100 in²/24 hours at 1 atmosphere and RT, and/or O₂TR values of less than or equal to 0.001 cm³/100 in²/24 hours at 1 atmosphere and RT.

Methods of Manufacture

[0063] The inventive monolayer or multilayer film may be made by conventional processes. These processes to produce flexible films may include e.g. cast or blown film processes.

[0064] Unless specifically noted the polymers defined herein are "unmodified" by any intentional grafting or copolymerization with modifying moieties such as dienes, rubber moieties or acrylic acids. However, the polymers may contain chemicals or additives in small amounts (typically under 1% by weight based on the weight of the polymer) which are present as by-products of the polymer manufacturing process or otherwise added by polymer manufacturers including e.g. catalyst residues, antioxidants, stabilizers, antiblock materials and the like.

[0065] Reported and/or measured properties of suitable polymers including those used in the examples below, and of polymers used in the comparative examples are presented in Tables A-C, below. In these tables, Exact and Escorene polymers are the commercial designations of polymers available from Exxon Chemical Company of Houston, Tex., U.S.A. Affinity and Attane polymers are the commercial designations of polymers available from Dow Chemical Company of

Midland, Mich., U.S.A. Surlyn and Elvax are the commercial designations of polymers available from Dupont, U.S.A.

[0066] Metal foils and metalized films are also contemplated. One or more functional properties may be contributed by one or more layers including desired levels of heat sealability, optical properties e.g. transparency, gloss, haze, abrasion resistance, coefficient of friction, tensile strength, flex crack resistance, puncture resistance, abrasion resistance, printability, colorfastness, flexibility, dimensional stability, barrier properties to gases such as oxygen, or to moisture, light of broad or narrow spectrum including e.g. uv resistance, etc. Preferred materials for use as container walls, pouch films, lidstock, include nylons, polyesters, polystyrenic polymers, and polyolefin e.g. ethylene or propylene homopolymers or copolymers, or mixtures thereof in any number of layers, particularly, but not limited to, one to nine or 14 layers or more. preferred polyolefins include ethylene homopolymers or copolymers and may include low, medium, high and ultra-low or ultra-high density polymers. Examples are high density polyethylene (HDPE), ethylene alpha-olefin copolymers (EAO) preferably utilizing butene-1, hexene-1, or octene-1 comonomer with a predominate ethylene comonomer portion) and including e.g. linear low density polyethylene (LLDPE), very low density polyethylene (VLDPE), plastomers, elastomers, low density polyethylene (LDPE) copolymers of ethylene and polar groups such as vinyl acetate or ethyl acrylate e.g. ethylene vinyl acetate (EVA) or ethylene methyl acrylate (EMA) or ethylene acrylic acid copolymer (EAA), functional group modified polymers including e.g. anhydride modified EAOs. Propylene homopolymers and copolymers including polypropylene and propylene ethylene copolymer are useful. Gas diversion or container wall structures may also include a metal foil and may be a metal foil laminate with metal foil and a polymeric layer such as nylon. It may also be a metal foil laminate with an outer layer of polyethylene terephthalate, a core layer of metal foil and an inner layer of polyethylene. In this arrangement, the polyethylene terephthalate layer serves as a protective layer to the foil, and the polyethylene layer facilitates sealing. The foil is an excellent barrier to materials organisms, oxygen, moisture and light.

[0067] In accordance with the present invention, the inventive packaging film may utilize a gas barrier layer such as aluminum foil, polyvinylidene chloride copolymers such as saran, or ethylene vinyl alcohol copolymers which provide high barriers to gas permeability.

[0068] In accordance with the present invention, the inventive packaging film may utilize a moisture barrier layer such as aluminum foil, polyvinylidene chloride copolymers such as saran, or polyolefin materials such as LDPE which impede moisture vapor permeation.

[0069] Adhesives useful in the present invention include permanent adhesives, modified polymer adhesives and polymer resins commonly available from many commercial sources. It is contemplated that acrylic and anhydride modified polymers may be employed as well as many adhesives which may be selected depending upon other material selections for other functional layers such as the oxygen and/or moisture barrier layer(s) as well as the exterior abuse resistant or protecting layer as well as the required COC layer.

[0070] Additives and processing aides; natural and synthetic colorants, pigments and dyes; fillers such as calcium

carbonate or carbon black, antimicrobial agents may be incorporated into or coated on one or more layers of the multilayer films of the present invention.

[0071] Film Thickness

[0072] Preferably, the packaging film has a total thickness of less than about 10 mils, more preferably the film has a total thickness of from about 1.0 to 10 mils (25-250 microns (μ)). Advantageously many embodiments may have a thickness from about 1 to 5 mils, with certain typical embodiments being from about 2 to 3.5 mils. For example, entire multilayer films or any single layer of a multilayer film can have any suitable thicknesses, including 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 mils, or any increment of 0.1 or 0.01 mil therebetween. Although suitable films for packaging drug patches as thick as 4 mils (101.6 microns) or higher, or as thin as 1 mil (25.4 microns) or less may be made, it is expected that the most common films will be between about 2-4 mil (51-102 microns). Especially preferred for use as films for transdermal patch packaging are films where the multilayer film has a thickness of between about 2 to 3 mils (50.8-76.2 microns). Such films may have good abuse resistance and machinability.

[0073] Referring now to the Drawings, FIG. 1 is an embodiment of the invention and illustrates a package container wall such as a pouch wall of multilayer composition and containing an oxygen and water barrier layer and scalping resistant article contact layer.

[0074] Typical contents for various embodiments of the inventive container may include, for example, transdermal patches, thin strips of dissolvable material for oral administration, as well as articles for collecting or administering a physiologically active substance e.g. a microdiffusion cassette.

[0075] Exemplary of commercially available LDPE resin suitable for use in the present invention includes, but are not limited to Equistar 216-000 LDPE resin. Exemplary of commercially available EAA resin for use in the present invention includes, but is not limited to Dupont 3990-L, which is supplied by Dupont de Nemours. Exemplary of commercially available ionomer resin for use in the present invention includes, but is not limited to Dupont 1652-1 Surlyn, which is supplied by Dupont de Nemour. Exemplary of commercially available EAA resin for use in the present invention includes, but is not limited to Dupont 3990-L, which is supplied by Dupont de Nemours.

[0076] The mLLDPE layer used in the examples was a blend of 80% LDPE comprising and 20% mLLDPE.

[0077] Exemplary of commercially available LDPE resin for use in the present invention includes, but is not limited to Dow 4012 LDPE which is supplied by Dow Chemical Co. of Midland, Mich., USA.

[0078] Exemplary of commercially available mLLDPE resin for use in the present invention includes, but is not limited to Exxon Exact 3040 mLLDPE resin, which is supplied by Exxon.

[0079] Exemplary of commercially available COC resin for use in the present invention includes, but is not limited to Topas 8007F-400, which is supplied by Topas Advanced Polymers.

[0080] The containers e.g. a pouch can further include a tearing aid or tear initiator such as a notch. Examples of tearing aids or tear initiators such as notches, slits, perforations, surface roughened portions, etc., are described in U.S. Pat. Nos. 4,778,058; 3,608,815; 4,834,245; 4,903,841; 5,613,

779; 5,988,489; 6,102,571; 6,106,448; 6,541,086; 7,470,062; and 7,481,581. Such tear initiators may be used on one or more edges of the inventive pouch and package.

[0081] Advantageously the tear initiator may be used with scoring e.g. mechanical or laser scoring of one or more layers, preferably the other abuse resistance layer, to create a tear directing line which facilitates opening. Prior art films used for packaging transdermal patches which utilize polyacrylonitrile as the patch contact surface layer (sealant layer) have undesirably poor tear properties, being very susceptible to delamination upon attempts to tear open even with scoring. These packages typically must use scissors or a knife for opening. Beneficially, the present invention has excellent tear properties and when used with a score line may be manually opened in a clean, non-delaminating fashion without use of scissors or other cutting implements. This easy to open feature of the present invention may be coupled with child resistant packaging technology such as that described in pending patent application number PCT/US2013/022101, which is hereby incorporated by reference in its entirety, to provide a child resistant package which is simultaneously easy to open by an adult.

[0082] Experimental results and reported properties are based on the following test methods or substantially similar test methods unless noted otherwise.

Oxygen Gas Transmission Rate (O_2 GTR): ASTM D-3985-81

Water Vapor Transmission Rate (WVTR): ASTM F 1249-90

Gauge: ASTM D-2103

[0083] Melt Index (M.I.): ASTM D-1238. Condition E (190° C.) (except for propene-based (>50% C_3 content) polymers tested at Condition TL (230° C.))

Melting point: ASTM D-3418, DSC with 5° C./min heating rate

Glass transition temperature T_g : ASTM D3418

Gloss: ASTM D-2457, 45° angle

Nicotine Direct Contact Test

[0084] Ten pouches are made with each test film by heat sealing together two pieces of the sample film each measuring 3x3.5 inches on three sides with the same article contact surface facing each other. Next, 50 μ l of pure nicotine is placed on a 1x1.25 inch piece of blotter paper and the blotter paper is placed inside the pouch which is then heat sealed.

[0085] The pouches are stored at 100° F. and 20% RH and two pouches of each film structure are tested at reported intervals e.g. days 1, 2, 8, 15 and 31. After the allotted time, two pouches are opened by cutting an end seal, and the blotters removed. The blotterless pouches are rinsed with distilled water to remove any liquid nicotine that might be present on the surface of the sealant and excess water is removed from the pouches by shaking. Next, 5 ml of isopropanol spiked with an internal standard (propylene glycol n-propyl ether) is placed in each pouch which is then resealed with heat seals. The resealed pouches are placed on a shaker table for 90 minutes to facilitate nicotine extraction from the sealant. Finally, the pouch extracts are analyzed by gas chromatography and the amount of eluted nicotine is calculated for each pouch.

Nicotine Vapor Test

[0086] Ten pouches are made with each test film by heat sealing together two pieces of the sample film each measuring 3×3.5 inches on three sides with the same article contact surface facing each other. Next, 50 µl of pure nicotine is placed on a 1×1.25 inch piece of blotter paper. The blotter paper is then wrapped in perforated foil having approximately 20 needle perforations per side. The foil wrapped blotter paper is placed inside the pouch which is then hermetically sealed. The perforated foil wrapper prevents direct contact of the blotter absorbed nicotine with the sealant layer of the film.

[0087] The blotter containing pouches are stored at 100° F. and 20% Relative Humidity (RH). Two pouches of each film structure are tested at recorded intervals e.g. days 1, 2, 8, 15 and 31 as follows. After the allotted time, two pouches are opened by cutting an end seal, and the foil covered blotters are removed. Next, 5 ml of isopropanol, spiked with an internal standard (propylene glycol n-propyl ether), is placed in each pouch and each blotterless pouch is resealed with heat seals. The resealed pouches are then placed on a shaker table for 90 minutes to facilitate nicotine extraction from the sealant. Finally, the pouch extracts are analyzed by gas chromatography and the amount of eluted nicotine is calculated for each pouch.

[0088] Eluted nicotine values are measured by the methods described above or tests similar thereto, unless otherwise specified.

[0089] Following are examples given to illustrate the invention, but these examples should not be taken as limiting the scope. All percentages are by weight unless indicated otherwise.

[0090] Films of 6, 7, 8, 9 or more layers are contemplated. The inventive multilayer films may include additional layers or polymers to add or modify various properties of the desired film such as heat sealability, interlayer adhesion, wrinkle resistance, puncture resistance, printability, toughness, gas and/or water barrier properties, abrasion resistance, printability, and optical properties such as gloss, haze, freedom from lines, streaks or gels. These layers may be formed by any suitable method including coextrusion, extrusion coating and lamination.

[0091] Unless otherwise noted, the thermoplastic resins utilized in the present invention are generally commercially available in pellet form and, as generally recognized in the art, may be melt blended or mechanically mixed by well-known methods using commercially available equipment including tumblers, mixers or blenders. Also, if desired, well known additives such as processing aids, slip agents, anti-blocking agents and pigments, and mixtures thereof may be incorporated into the film or applied to one or more surfaces thereof, e.g. by blending prior to extrusion, powdering, spraying, contact roller application, etc. Typically the resins and any desired additives are mixed and introduced to an extruder where the resins are melt plastified by heating and then transferred to an extrusion (or coextrusion) die. Extruder and die temperatures will generally depend upon the particular resin or resin containing mixtures being processed and suitable temperature ranges for commercially available resins are generally known in the art, or are provided in technical bulletins made available by resin manufacturers. Processing temperatures may vary depending upon other processing parameters chosen.

Examples 1-5

[0092] Examples 1-4 are comparative examples (not of the invention). Example 5 is an example according to the present invention. In all of the examples, a multilayer film is provided having a base film and connected sealant film. The sealant film has a surface layer which is designed to contact the article to be packaged e.g. a transdermal patch article, and to permit heat sealing of the multilayer film to form a container such as a pouch. The EAA/LDPE/COC sealant layer of the invention and the comparative sealant layers were either extrusion coated or adhesively laminated to In all of the examples 1-5, a multilayer base film having the following structure: OPET/Primer/PE/EAA/Foil was made and only the connected sealant film was varied.

Base Film

[0093] The base film was comprised of five layers having an ordered structure of:

/Layer 1/Layer 2/Layer 3/Layer 4/Layer 5/corresponding to: /exterior layer 1/primer layer 2/bulk layer 3/adhesive layer 4/O₂ layer 5/: or more particularly,

/OPET/PE/LDPE/EVA/Al Foil/.

[0094] Layer 1 was a commercially available 0.92 mil, biaxially oriented polyethylene terephthalate (OPET) film corona treated on one side. The treated OPET film received a second corona treatment on the previously treated side prior to receiving an anchor coating of a water-based polyethyleneimine (PEI) primer (Layer 2) that was contact coated onto the corona treated side of the OPET film and dried just prior to lamination of the OPET film to 0.35 mil aluminum foil (Layer 5) using a coextrusion of LDPE (Layer 3) and EAA (Layer 4). Layers 3 and 4 were produced by the two-layer coextrusion of LDPE and EAA. The anchor coated side of the OPET film was laminated to 0.35 mil aluminum foil with a coextrusion of LDPE and EAA. The LDPE was a blend of 87.5 wt. % LDPE laminate resin and 12.5 wt. % of a white colorant in a carrier resin. The oxygen and moisture barrier was provided by a commercially available aluminum foil.

Comparative Example 1

[0095] In example 1, a sealant film of ionomer was extrusion coated onto a five layer base film made as described above. The aluminum foil surface of the multilayer base film having the structure OPET/primer/LDPE/EAA/foil was corona treated and then extrusion coated with ionomer. The ionomer used was a zinc salt of ethylene-methacrylate acid copolymer commercially available under the trademark Surlyn® 1652-1 and having a reported density of 0.940 g/cm³ and melt index of 4.5 g/10 min.

[0096] The resultant six layer, multilayer film had the following structure: 0.92 mil OPET/primer/coex (0.42 mil LDPE/0.1 mil EAA)/0.35 mil foil/1.0 mil ionomer, and had a total nominal thickness of 2.8 mils (71 microns).

Comparative Example 2

[0097] The base film for example 2 was produced in the same manner as for example 1 except that the aluminum foil was not corona treated prior to the addition of the sealant film. In comparative example 2, a three-layer coextrusion of: EAA; LDPE; and an 80:20 wt % blend of LDPE:mLLDPE was extrusion coated onto the aluminum foil surface of the mul-

tilayer base film with the EAA layer adhered to and in direct contact with the aluminum foil. The resultant multilayer film had the following structure 0.92 mil OPET/primer/(0.42 mil LDPE/0.1 mil EAA)/0.35 mil foil/0.17 mil EAA/0.65 mil LDPE/0.43 mil LDPE:mLLDPE and a total thickness of 3.04 mils (77.2 microns).

Comparative Example 3

[0098] The base film for example 3 was produced in the same manner as for example 2. In comparative example 3, the sealant film was a commercially available, corona treated, cast APET film. The APET film received an additional corona treatment prior to adhesive lamination. The base and sealant films were laminated by coating the aluminum foil surface of the multilayer base film having the structure OPET/primer/

minum foil surface of the multilayer base film to produce an eight layer film having the structure: 0.92 mil OPET/primer/0.42 mil LDPE/0.1 mil EAA/0.35 mil foil/0.17 mil EAA/0.65 mil LDPE/0.43 mil COC and a total thickness of 3.0 mils (76 microns). The inventive film is well suited to package articles for collecting or administering a physiologically active substance such as transdermal drug delivery patches, or oral dissolvable thin strips and has advantageous moisture barrier, oxygen barrier, and low scalping properties as discussed below. The resultant multilayer film was tested for various properties which are reported below.

Scalping Tests for Examples 1-5

[0101] Each of the films made in Examples 1-5 were tested for nicotine scalping by a "Nicotine Direct Contact Test" and a "Nicotine Vapor Test". Properties are reported in Table 1 below.

TABLE 1

Ex.	Sealant Layer	Ave. Sealant Thickness (mil)	Nicotine Direct Contact Test Amount of Eluted Nicotine (mg)					Nicotine Vapor Test Amount of Eluted Nicotine (mg)				
			Day 1	Day 2	Day 8	Day 15	Day 31	Day 1	Day 2	Day 8	Day 15	Day 31
1	Ionomer	1.0	17.1	15.3	16.7	24.0	22.0	8.5	11.9	15.8	25.2	23.7
2	LDPE:mLLDPE 80:20 wt. % blend	0.43	10.5	10.8	13.3	17.0	15.8	5.76	7.85	11.5	17.2	16.2
3	APET	2	12.6	10.5	12.0	13.1	11.2	1.73	2.47	Leak in Pouch	Leak in Pouch	2.3
4	polyacrylonitrile	1.5	0.05	0.00	0.00	0.03	0.03	0.21	0.36	0.49	0.70	1.08
5	COC	0.43	2.08	3.47	1.42	3.12	2.03	0.94	1.26	1.95	2.42	1.26

LDPE/EAA/foil with a 2-part urethane adhesive using an analox roller followed by laminating contact to a corona retreated cast APET film. The resultant 7 layer film had the following structure: 0.92 mil OPET/primer/0.42 mil LDPE/0.1 mil EAA)/0.35 mil foil/0.08 mil adhesive/2 mil APET (inside) and a total thickness of 3.9 mils (99 microns).

Comparative Example 4

[0099] The base film for example 4 was produced in the same manner as for example 2 except that the LDPE/EAA coextrusion was applied slightly thicker. In comparative example 4, the sealant film was a corona treated polyacrylonitrile film. The polyacrylonitrile film received an additional corona treatment just prior to lamination. The aluminum foil surface of the multilayer base film having the structure OPET/primer/LDPE/EAA/foil was then coated with a 2-part urethane adhesive using an analox roller and the structure was adhesively laminated to the corona retreated polyacrylonitrile film. The resultant multilayer film had the following structure (outside) 0.92 mil OPET/primer/0.56 mil LDPE/0.1 mil EAA)/0.35 mil foil/0.07 mil Adhesive/1.5 mil Barex (inside) and a total thickness of 3.5 mil.

Example 5

Of the Invention

[0100] The film structure in Example 5 is exemplary of a film according to the present invention. The base film for example 5 was produced in the same manner as for comparative example 2. In this example, the sealant film was a three-layer coextrusion of EAA, LDPE and Ethylene-norbornene copolymer (COC) which was extrusion coated onto the alu-

[0102] A single roll web of pouch film is placed on a packaging machine and folded together and heat sealed and severed to form heat sealed pouches. Two side sealed pouches with a folded third side are used to package an article by a manufacturer or packager who places a product in the pouch, and completes the final seal to produce a hermetically sealed package containing for example: a transdermal drug delivery patch; an oral dissolvable thin strip containing a drug, flavorant, antimicrobial agent, odorant, and/or microbiologically active ingredient or combination thereof; or an article for collecting or administering a physiologically active substance.

[0103] Referring to the drawings, FIG. 1 is a schematic view of the layers of the film according to the invention. Layers 1-8 correspond to the sequential layers from the outside to surface article contact layer.

[0104] Various embodiments have been described above. Although the invention has been described with reference to these specific embodiments, the descriptions are intended to be illustrative and are not intended to be limiting. Various modifications and applications may occur to those skilled in the art without departing from the true spirit and scope of the invention as defined in the appended claims.

What is claimed is:

1. A drug scalping resistant, flexible, multilayer packaging film comprising:

- (a) a drug contact layer having at least 90 wt. % of an ethylene norbornene copolymer or derivative thereof having a glass transition temperature of from 65 to 110° C.;
- (b) a polyolefin bulk layer;
- (c) a first intermediate adhesive layer;

(d) an oxygen barrier layer having an oxygen transmission rate of less than less than $0.01 \text{ cm}^3/100 \text{ inches}^2/24 \text{ hours}$ at 1 atmosphere and 23° C. ;

(e) a second intermediate adhesive layer; and

(f) an exterior protective layer comprising a polymer selected from the group consisting of paper, oriented polyester, amorphous polyester, polyamide, polyolefin, nylon, polypropylene, or copolymers, blends or derivatives thereof;

wherein said multilayer film has the following properties: a WVTR of less than $0.01 \text{ g}/100 \text{ inches}^2$ per 24 hours at Room Temperature (RT) (23° C.) and 1 atmosphere.

2. A multilayer film as defined in claim 1, wherein: said contact layer comprises at least 95 wt. % ethylene norbornene copolymer or derivative thereof.

3. A multilayer film as defined in claim 1, wherein: said contact layer consists essentially of ethylene norbornene copolymer or derivative thereof.

4. A multilayer film as defined in claim 1, wherein said film is formed into a flexible container and further comprises a transdermal patch sealed therein.

5. A multilayer film as defined in claim 4, wherein said patch is a nicotine or fentanyl drug delivery patch.

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