THIN FILM WITH NON-SELF-AGGREGATING UNIFORM HETEROGENEITY

FIELD OF THE INVENTION

[0001] The invention relates to rapidly dissolving films and methods of their preparation. The films may also contain an active ingredient that is evenly distributed throughout the film. The even or uniform distribution is achieved through a controlled drying process that reduces aggregation or conglomeration of the components in the film.

BACKGROUND OF THE RELATED TECHNOLOGY

[0002] Active ingredients such as drugs or pharmaceuticals, may be prepared in a tablet form to allow for accurate and consistent dosing. However, this form of preparing and dispensing medications has many disadvantages including that a large proportion of adjuvants that must be added to obtain a size able to be handled, that a larger medication form requires additional storage space, that dispensing includes counting the tablets which has a tendency for inaccuracy. In addition, many persons, around 28%, have difficulty swallowing tablets. Difficulty swallowing tablets is particularly an issue where tablets such as controlled release drugs may not be crushed to allow for an easier administration of the drug, e.g. mixing the crushed tablet with food.

[0003] Some have proposed that films may be used to carry active ingredients such as drugs, pharmaceuticals, and the like. However, historically films have suffered from a number of unfavorable characteristics that have not allowed them to be used in practice.

[0004] Films that incorporate a pharmaceutically active ingredient are disclosed in U.S. Patent No. 4,136,145 to Fuchs, et al. ("Fuchs"). These films may be formed into a sheet, dried and then cut into individual doses. The Fuchs disclosure alleges the fabrication of a uniform film, however, examination of films made in accordance with the process disclosed in Fuchs reveals that such films suffer from the aggregation or conglomeration of particles, i.e., self-aggregation, making them inherently non-uniform. This result is believed to be related to Fuchs'

process which uses relatively long drying times, thereby permitting intramolecular attractive forces, conventional forces and the like to encourage such agglomeration. When large dosages are involved, there is a need to be especially attentive to ensuring an adequate amount of the active is present in the delivery vehicle. For example, where a large amount of active is used, a small change in the dimensions of the film would lead to a large difference in the amount of active per film. Failure to achieve a high degree of accuracy with respect to the amount of active ingredient in the cut film can be harmful to the patient.

[0005] The problems of self-aggregation leading to non-uniformity of a film, were addressed in U.S. Patent No. 4,849,246 to Schmidt ("Schmidt"). Schmidt specifically pointed out that the methods disclosed by Fuchs did not provide a uniform film and recognized that that the creation of a non-uniform film necessarily prevents accurate dosing, which is especially important in the pharmaceutical area. Schmidt abandoned the idea that a mono-layer film may provide an accurate dosage form and instead attempted to solve this problem by forming a multi-layered film. Not only does Schmidt fail to provide a uniformly distributed film, he proposed a multi-step process that is not practical for commercial use.

[0006] Two other U.S. Patents directly addressed the problems that Fuchs had regarding that the uniformity of films was affected by the self-aggregation of particles that occurred during the drying of the film. In an attempt to overcome non-uniformity, U.S. Patent 5,629,003 to Horstmann et al. and U.S. Patent 5,948,430 to Zerbe et al. added gel formers and polyhydric alcohols respectively, to increase the viscosity of the film before it is dry in an effort to reduce aggregation of the components in the film. Both of these methods have the disadvantage of requiring additional components which translates to additional cost and manufacturing steps. Furthermore, both methods employ the use the conventional time-consuming drying methods such as a high-temperature air-bath using a drying oven, drying tunnel, vacuum drier, or other such drying equipment. The long length of drying time aids in promoting the aggregation of the active and other adjuvant. Such processes also run the risk of exposing the active, i.e., a drug, or vitamin C, or other components to prolonged exposure to moisture and elevated temperatures which may render it ineffective or even harmful.

[0007] Therefore, there is a need for compositions which can be forward into film products, which use a minimal number of materials or components, and which provide a substantially non-self-aggregating uniform heterogeneity throughout the area of the films. Desirably, such films are produced through a selection of polymer that will provide a desired viscosity, a specific film-forming process such as reverse roll coating, and a controlled, and desirably rapid, drying process which serves to maintain the uniform distribution of non-self-aggregating components without the necessary addition of gel formers or polyhydric alcohols which are required in the products and for the processes of Horstmann and Zerbe.

SUMMARY OF THE INVENTION

[0008] In one aspect of the present invention, there is provided a film product that is formed by combining a polymer and a polar solvent, forming the combination into a film, and rapidly drying the film in order to maintain a non-self-aggregating uniform heterogeneity. The polar solvent may be water, a polar organic solvent, or a combination thereof. An active ingredient may be added to the polymer and water combination prior to the drying step. Alternatively, or in addition to rapidly drying the film, the polymer may be selected in order to provide a viscosity that maintains the non-self-aggregating uniform heterogeneity. Reverse roll coating technique may also be used to form the film.

[0009] In another aspect of the invention, there is a process for preparing a film with a substantially uniform distribution of components. The process includes the steps of combining a polymer component and water to form a uniformly distributed matrix. This matrix is then formed into a film and fed onto a surface having top and bottom sides where the bottom side is in substantially uniform contact with a water bath controlled at a temperature sufficient to dry the film. The matrix from which the film is formed may also include an active ingredient. Also, either alternatively, or in addition to rapidly drying the film, the polymer may be selected in order to provide a viscosity that maintains the non-self-aggregating uniform heterogeneity. Reverse roll coating technique may also be used to form the film.

[0010] A further aspect of the present invention is method of orally administering an active including the steps of:

(a) preparing a film by the steps of:

(i) combining a polymer, an active component, and water to form a material with a non-self-aggregating uniform heterogeneity;

(ii) forming the material into a film; and

(iii) drying the film in a sufficiently rapid time to maintain the non-self-aggregating uniform heterogeneity; and

(b) introducing the film to the oral cavity of a mammal.

[0011] An even further aspect of the present invention is method of introducing an active component to liquid including the steps of:

(a) preparing a film by the steps of:

(i) combining a polymer, an active component, and water to form a material with a non-self-aggregating uniform heterogeneity;

(ii) forming the material into a film; and

(iii) drying the film in a sufficiently rapid time to maintain the non-self-aggregating uniform heterogeneity; and

(b) placing the film into a liquid; and

(c) allowing the film to dissolve.

[0012] A still further aspect of the present invention provides a dosage form for the administration of an active including:

(a) a first layer including a film formed by the steps of:

(i) combining a polymer, an active component, and water to form a material with a non-self-aggregating uniform heterogeneity;

(ii) forming said material into a film; and

(iii) drying said film in a sufficiently rapid time to maintain said non-self-aggregating uniform heterogeneity; and

(b) a substantially non-water soluble second layer.

[0013] Another aspect of the present invention provides a method of preparing a dosage form for the administration of an active including the steps of:

(a) preparing a film by the steps of:

(i) combining a polymer, an active component, and water to form a material with a non-self-aggregating uniform heterogeneity;

(ii) forming the material into a film; and

(iii) drying the film in a sufficiently rapid time to maintain the non-self-aggregating uniform heterogeneity; and

(b) applying the film to a substantially non-water soluble support.

[0014] In still another aspect of the present invention there is provided another method of administering an active including the steps of:

(a) preparing dosage form by the steps of:

(i) combining a polymer, an active component, and water to form a material with a non-self-aggregating uniform heterogeneity;

(ii) forming the material into a film;

(iii) drying the film in a sufficiently rapid time to maintain the non-self-aggregating uniform heterogeneity; and

(iv) applying the film to a substantially non-water soluble support;

(b) removing the film from said support; and

(c) applying the film to the oral cavity of a mammal.

[0015] Another aspect of the invention provides a film product formed by the steps of:

(a) combining a polymer and a liquid carrier to form a material with a non-self-aggregating uniform heterogeneity;

(b) forming said material into a film; and

(c) removing said liquid carrier, for example, by evaporative methods or by permitting volatilization to occur at selected temperatures, from said film in a manner to maintain said non-self-aggregating uniform heterogeneity.

[0016] Also provided is a process for making a film having a substantially uniform distribution of components comprising:

DOCKET ALARM

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts

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

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

Advanced Docket Research

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

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

Analytics At Your Fingertips

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

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

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

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS
Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS
Sync your system to PACER to automate legal marketing.