Research and Development of Medicinal Products from Chemicals Extracted from Marijuana

Assoc.Prof.Dr. Narisa Kamkaen

College of Pharmacy, Rangsit University
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Timeline of cultural and medical milestones in cannabis
Prescribing cannabis-based products for medicinal use

• The Advisory Council on the Misuse of Drugs (ACMD) thereafter concluded the first aspect of part 2 of the review.\(^2\)

• It also recommended that “cannabis-derived medicinal products of the appropriate standard” be moved out of Schedule 1 and, subject to further refinement of the definition of cannabis-based products for medicinal use, into Schedule 2.

• Synthetic cannabinoids were specifically excluded from this and reserved for further consideration.
Prescribing cannabis-based products for medicinal use

- The Government has defined a cannabis-based product for medicinal use in humans as: “a preparation or other product, other than one to which paragraph 5 of part 1 of Schedule 4 applies, which—

  (a) Is or contains cannabis, cannabis resin, cannabinol or a cannabinol derivative (not being dronabinol or its stereoisomers);

  (b) Is produced for medicinal use in humans; and—

  (c) is—

  (i) a medicinal product, or

  (ii) a substance or preparation for use as an ingredient of, or in the production of an ingredient of, a medicinal product;”
Medicinal Cannabis Products Cannabis for human therapeutic use is regulated as a medicine in Australia.

The term 'medicinal cannabis products' covers a range of cannabis preparations intended for therapeutic use, including pharmaceutical cannabis preparations, such as oils, tinctures and other extracts.

Some examples of medicinal cannabis products that may be available through approved suppliers in Australia are listed below.

Products must be legally produced and manufactured to appropriate quality standards.

Commonwealth approval to supply, and where necessary import a medicinal cannabis product is granted by the Therapeutic Goods Administration (TGA) and the Office of Drug Control (ODC).

EU drugs agency publishes its first report on the medical use of cannabis

Cannabis and cannabinoids used for medical purposes — a broad typology

<table>
<thead>
<tr>
<th>Medicinal products with marketing authorisation</th>
<th>Examples of medicinal products and their active ingredients</th>
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<tr>
<td>Cesamet and Canemes</td>
<td>Marinol and Syndros</td>
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<tr>
<td>Containing nabilone</td>
<td>Containing dronabinol</td>
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<tr>
<td>Synthetic cannabinoid similar to THC</td>
<td>Synthetic THC</td>
</tr>
<tr>
<td></td>
<td>Sativex</td>
</tr>
<tr>
<td></td>
<td>Containing nabiximols</td>
</tr>
<tr>
<td></td>
<td>Plant-based; approx. equal quantities CBD/THC</td>
</tr>
<tr>
<td></td>
<td>Epidiolex</td>
</tr>
<tr>
<td></td>
<td>Containing cannabidiol</td>
</tr>
<tr>
<td></td>
<td>Plant-based CBD</td>
</tr>
</tbody>
</table>

Cannabis preparations

<table>
<thead>
<tr>
<th>Raw cannabis</th>
<th>Magistral preparations</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Variable in THC/CBD composition</td>
<td></td>
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### Summary of the evidence for the medical use of cannabis and cannabinoids

<table>
<thead>
<tr>
<th>Disease/symptoms</th>
<th>Products tested</th>
<th>Strength of evidence</th>
<th>Limitations</th>
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<tbody>
<tr>
<td>Nausea and vomiting associated with cancer chemotherapy</td>
<td>Cannabinoids</td>
<td>Weak</td>
<td>Few studies testing against newer, more effective anti-emetics.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Newer chemotherapy regimens produce less nausea.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Little evidence available about use in other types of nausea.</td>
</tr>
<tr>
<td>Appetite stimulant in patients with AIDS-related wasting</td>
<td>Dronabinol/THC</td>
<td>Weak</td>
<td>Fewer AIDS-related cases available to treat now.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Little evidence available about use to stimulate appetite in people with other conditions.</td>
</tr>
<tr>
<td>Muscle spasm in patients with multiple sclerosis</td>
<td>Nabiximols</td>
<td>Moderate</td>
<td>Patients report reductions, but more limited impact on clinician ratings.</td>
</tr>
<tr>
<td>CNCP, including neuropathic pain</td>
<td>Cannabis and cannabinoids</td>
<td>Moderate</td>
<td>Small (but statistically significant) effect compared with placebo.</td>
</tr>
<tr>
<td>Palliative care for cancer</td>
<td>Cannabinoids</td>
<td>Insufficient</td>
<td>Larger, better-designed trials are needed.</td>
</tr>
<tr>
<td>Intractable childhood epilepsy</td>
<td>CBD</td>
<td>Moderate</td>
<td>Evidence for use in adjunctive therapy in people with Dravet or Lennox-Gastaut syndrome. More studies are needed to look at dosage, interactions and use in people with other forms of epilepsy.</td>
</tr>
<tr>
<td>Other medical uses, such as sleep disorders, anxiety disorders, depression, degenerative neurological disorders, and inflammatory bowel disease</td>
<td>Cannabis or cannabinoids</td>
<td>Insufficient</td>
<td>Some evidence for short-term effects in some conditions (e.g. sleep disorders) but larger, better-designed trials are needed, with longer follow-up.</td>
</tr>
</tbody>
</table>

Medical marijuana demand, imports continue to climb in Germany

Medical marijuana demand, imports continue to climb in Germany

Growth slows for German medical cannabis market in third quarter

What cannabis shortage? Canada has ‘sufficient supply,’

https://mjbizdaily.com/canadian-government-says-country-has-sufficient-marijuana-supply-to-meet-demand/
Pharmaceutical Drugs Based on Cannabis

• 1. Sativex
  Manufacturer: GW Pharmaceuticals (GWPH on NASDAQ)
  - Cannabis-Related Properties
    Mouth spray whose chemical compound is derived from natural extracts of the cannabis plant. Sativex contains two cannabinoids: THC (delta-9-tetrahydrocannabinol) and CBD (cannabidiol).
  - Suggested Medical Use
    Treatment of neuropathic pain and spasticity in patients with Multiple Sclerosis (MS); Analgesic treatment in adult patients with advanced cancer who experience moderate to severe pain.

• 2. Dronabinol / Marinol
  Manufacturer: Unimed Pharmaceuticals, a subsidiary of Solvay Pharmaceuticals
  
  • Cannabis-Related Properties
    Synthetic Delta-9 THC.
  
  • Suggested Medical Use
    Treatment of nausea and vomiting for patients in cancer treatment; appetite stimulant for AIDS patients; analgesic to ease neuropathic pain in multiple sclerosis patients.
Pharmaceutical Drugs Based on Cannabis

3. Nabilone / Cesamet
Manufacturer: Valeant Pharmaceuticals International (VRX on NASDAQ)

- Cannabis-Related Properties
  Synthetic cannabinoid similar to THC.

- Suggested Medical Use
  Treatment of nausea and vomiting in patients undergoing cancer treatment.

4. Dexanabinol
Manufacturer: Solvay Pharmaceuticals (acquired by Abbott Laboratories in 2010; ABT on NASDAQ)

• Cannabis-Related Properties
Synthetic non-psychotropic cannabinoid that blocks NMDA receptors and COX-2 cytokines and chemokines.

• Suggested Medical Use
Neuroprotective (protects brain from damage) for use after cardiac surgery; regain memory and other high-level function following Traumatic Brain Injury (TBI); possible future use as an anti-cancer drug.

Pharmaceutical Drugs Based on Cannabis

5. CT-3 (ajulemic acid)
Manufacturer: Indevus Pharmaceuticals (IDEV on NASDAQ)

Cannabis-Related Properties
Synthetic, more potent analog of THC metabolite THC-11-oic acid.

Suggested Medical Use
Treatment of spasticity and neuropathic pain in MS patients; anti-inflammatory properties may help relieve pain from arthritis

Cannabinoid formulations

- US8808734B2: PENDING
- UNITED STATES OF AMERICA

Abstract
- The present invention provides stable, fast-acting liposomal and micelle formulations of cannabinoids that are suitable for pharmaceutical and nutraceutical applications.
Cannabinoid formulations

- US8808734B2: PENDING
- UNITED STATES OF AMERICA
- Claims:
  - 1. A liposomal suspension of one or more cannabinoids or cannabinoid analogues, wherein the concentration of cannabinoids or cannabinoid analogues in the liposomal suspension is 50 g/liter, and wherein the bilayer of the liposomes comprises about 26% phosphatidylcholine, about 10% phosphatidylethanolamine, about 13% phosphonophospholipids, and about 1% of other phospholipids.
  - 2. The liposomal suspension of claim 1, wherein the one or more cannabinoids or cannabinoid analogues are a natural compound, a synthetic compound, a semi-synthetic compound, or mixtures thereof.

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Cannabinoid formulations

- US8808734B2: PENDING
- UNITED STATES OF AMERICA
- Claims:
  - 3. The liposomal suspension of claim 2, wherein the one or more cannabinoids or cannabinoid analogues are selected from the group consisting of cannabinol, cannabidiol, Δ9-tetrahydrocannabinol, Δ8-tetrahydrocannabinol, 11-hydroxy-tetrahydrocannabinol, 11-hydroxy-Δ9-tetrahydrocannabinol, levonatradol, Δ11-tetrahydrocannabinol, tetrahydrocannabivarin, dronabinol, amandamide, nabilone, and combinations thereof.
  - 4. The liposomal suspension of claim 1, wherein the liposomes have an average diameter size from about 200 to about 400 nm.

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Cannabinoid formulations

FIG. 1 provides an oil immersion image of a micelle suspension stained with fast blue as seen through a red filter.

https://patents.google.com/
Cannabinoid formulations

FIG. 2 provides an oil immersion image of an unstained liposomal suspension.
FIG. 3 provides an oil immersion image of a liposomal suspension stained with fast blue as seen through a red filter. The stain condensates on the outer liposome membrane.
The invention relates to pharmaceutical formulations, and more particularly to formulations containing cannabinoids for administration via a pump action spray.

In particular, the invention relates to pharmaceutical formulations, for use in administration of lipophilic medicaments comprising one or more cannabinoids via mucosal surfaces, comprising: at least one lipophilic medicament which comprises one or more cannabinoids, a solvent and a co-solvent, wherein the total amount of solvent and co-solvent present in the formulation is greater than 55 % wt/wt of the formulation, the formulation is absent of a self emulsifying agent and/or a fluorinated propellant, and the cannabinoid(s) is/are present in the formulation in an amount greater than 10 mg/ml.
Cannabinoid liquid formulations for mucosal administration

- EP1542657A1: ACTIVE
- EUROPEAN PATENT OFFICE
- Claims:
  1. A liquid pharmaceutical formulation, for use in the administration of a lipophilic medicament comprising one or more cannabinoids via a mucosal surface, comprising: a lipophilic medicament comprising one or more cannabinoids, a solvent and a co-solvent, wherein the total amount of solvent and co-solvent present in the formulation is greater than 55% wt/wt of the formulation, the formulation is absent of a self emulsifying agent and/or a fluorinated propellant, and the cannabinoid(s) is/are present in the formulation in an amount greater than 10 mg/ml.
A method for optimizing the therapeutic effects provided by CBD on the one hand, and the psychoactive effects provided by THC on the other hand, in a sublingual medicament, the method includes the steps of obtaining a concentrated extract of cannabis in which the concentration of CBD is known and the concentration of THC is known, formulating a hydrophilic mixture containing ingredients such as sugar, corn syrup, xylitol, purified water, organic flavorings, coconut oil, and concentrated extract of cannabis, wherein the amount of CBD is as high as possible and where the amount of THC is precisely controlled, forming lozenges, and administering the medicament.
Medical cannabis lozenges and compositions thereof

- US9504723B2
- UNITED STATES OF AMERICA: ACTIVE
- Claims:
  - 1. A lozenge for sublingual administration of a medicament consisting essentially of heat decarboxylated CO2-extracted *cannabis* sativa oil, heat decarboxylated CO2-extracted *cannabis* indica oil, xylitol and an ingredient selected from the group consisting of sugar, corn syrup, flavorings, coloring agents, coconut oil, purified water and mixtures thereof, the lozenge having a mass of between 2 grams and 15 grams, wherein the lozenge contains a minimum of 25 mg of cannabidiol and a maximum of 40 mg of tetrahydrocannabinol.

https://patents.google.com/
• **Claims:**

• 2. A method for minimizing the psychoactive effects of tetrahydrocannabinol in a therapeutic treatment of a human patient, the method consisting essentially of:

• a) formulating a lozenge consisting essentially of heat decarboxylated CO2-extracted *cannabis* sativa oil, heat decarboxylated CO2-extracted *cannabis* indica oil, xylitol and an ingredient selected from the group consisting of sugar, corn syrup, flavorings, coloring agents, coconut oil, purified water and mixtures thereof, the lozenge having a mass of between 2 grams and 15 grams, wherein the lozenge contains a minimum of 25 mg of cannabidiol and a maximum of 40 mg of tetrahydrocannabinol; and

• b) administering the lozenge of claim 1 sublingually to a human until the lozenge is dissolved in the human, thereby minimizing the psychoactive effects of tetrahydrocannabinol on the patient.
• **Claims:**
  
  3. A method of preparing a lozenge for sublingual administration of a medicament containing cannabidiol and tetrahydrocannabinol to a human patient, the method comprising the following steps: selecting a sativa *cannabis* in which the amount of cannabidiol and tetrahydrocannabinol is known;

  • selecting an indica *cannabis* in which the amount of cannabidiol and tetrahydrocannabinol is known;

  • heating the sativa *cannabis* and the indica *cannabis* to a temperature not higher than 190 degrees Fahrenheit for a period of time sufficient to cause decarboxylation of the cannabinoids contained therein;

  • extracting the sativa *cannabis* and the indica *cannabis* with CO2; and

  • formulating the lozenge with xylitol and an ingredient selected from the group consisting of sugar, corn syrup, flavorings, coloring agents, coconut oil, purified water and mixtures thereof, the lozenge having a mass of between 2 grams and 15 grams, whereby the lozenge contains a minimum of 25 mg of cannabidiol and a maximum of 40 mg of tetrahydrocannabinol.
Medical cannabis lozenges and compositions thereof

- US9504723B2
- UNITED STATES OF AMERICA: ACTIVE

As shown in FIG. 3, CBDOOS™ is one of the branded medical cannabis lozenges 200 available in the market now. It is made to achieve a gem or “see through” hard candy lozenge quality, appearance and texture.

- The formula for making 50 units consists of 2.25 cups of sugar, ⅔ cup of corn syrup, ¾ cup of purified water, 1 g of organic flavorings and lab determined proprietary amount of concentrated cannabis oil.

- In one embodiment, approximately 2.5 grams of cannabis oil will result in a product containing approximately 25 mg of CBDs per unit.

https://patents.google.com/
Medical cannabis lozenges and compositions thereof

- US9504723B2
- UNITED STATES OF AMERICA: ACTIVE

As shown in FIG. 4, GOOD-EZ™ is another branded medical cannabis lozenges of the present invention available in the market now.

It is made to be a sugar free xylitol based lozenge or crumble and are finished in a rose petal top, using 2.25 cups of USA sourced Birch non GMO Xylitol, ¼ cup of unpressed virgin organic coconut oil, 1 dram of organic flavorings and lab determined proprietary amount of concentrated cannabis oil.

In one embodiment, approximately 2.5 grams of cannabis oil will result in a product containing approximately 25 mg of CBDs per unit.
Medical cannabis lozenges and compositions thereof

- US9504723B2
- UNITED STATES OF AMERICA: ACTIVE
- FIG. 5 is a representation view of the CO2-extraction process used in the present invention. As shown, in a first step 502 cryogenic, liquid carbon dioxide (CO2) is injected into a pressure vessel 504 containing the whole cannabis plant material. The combination liquid CO2 and dissolved cannabinoids 506 exit the pressure vessel 504 and cross a pressure reducing valve 508 before entering separator 510. Recycled CO2 512 is re-pressurized across pump system 514, while the CO-2 extracted material is collected separately.
Inhalation of vapour of therapeutical substances, like e.g. cannabis extract

- WO2003037306A3
- WIPO (PCT)

**Abstract**

- A method of making a medicament which is a vapour comprising heating a composition to a temperature not exceeding 500 °C for a time of less than 10 seconds.
- The composition is non-volatile at 75 °C and generates a vapour free of pyrolysis products when heated in this way.
- The vapour is produced in a portion of air smaller than the mean respiratory tidal volume.
- A composition suitable for using in such a method is also disclosed.
The invention discloses fructus cannabis intestine-moistening pills and a preparation method thereof.


The fructus cannabis intestine-moistening pills has the advantages that the fructus cannabis intestine-moistening pills has an effect of relaxing bowels, can be used for treating symptoms of accumulated heat in the stomach and the intestines, chest and abdominal fullness and constipation, and are reasonable in cost, low in toxic and side effect, convenient to take, short in treatment course, capable of achieving batch production, suitable for various people and worthy of popularization.
Stable suppository formulations effecting bioavailability of Δ9-THC

- US5389375A: EXPIRED LIFETIME
- UNITED STATES OF AMERICA
- Abstract
  - Suppository formulations having long-term stability and containing readily bioavailable Δ9-THC derivatives.

https://patents.google.com/
Stable suppository formulations effecting bioavailability of Δ⁹-THC

Claim:

1. A long term stable suppository formulation comprising a therapeutically effective amount of at least one Δ⁹-THC prodrug ester derivative having the formula: ##STR3## where R is an hemiester of succinic acid in a pharmaceutically acceptable rectal suppository base wherein the suppository base affords long term stability of the Δ⁹-THC prodrug ester derivative contained in the suppository formulation such that greater than 90% of the original concentration of the hemisuccinate ester is retained for at least one year.
The present invention includes a transdermal patch which contains a pharmaceutically effective amount of a cannabinoid for delivery of the cannabinoid to the bloodstream of a user.

The patch may comprise the following components: a backing; and a skin-adhesive polymer matrix attached to one side of the backing, which includes a cannabinoid, a carrier agent, a terpene, and a permeation agent.

The cannabinoid is capable of diffusing from the matrix in the transdermal patch into the bloodstream of the user, and may be used in methods for treating a patient suffering from a condition such as pain, nausea and emesis, convulsions, muscle spasm, inflammation, depression, and cachexia.
Claim:

1. A transdermal patch comprising a pharmaceutically effective amount of a cannabinoid for delivery of the cannabinoid to the bloodstream of a user, said patch comprising:

   a) a backing
   b) a skin-adhesive polymer matrix attached to one side of the backing, said matrix

   comprising a cannabinoid, a carrier agent, an exogenous terpene, and a permeation agent;

   wherein the cannabinoid is capable of diffusing from the matrix in the transdermal patch into the bloodstream of the user.
The present invention includes a transdermal composition which contains a pharmaceutically effective amount of a cannabinoid for delivery of the cannabinoid to the bloodstream of a user. The composition may comprise the following components: a surfactant-lecithin organogel; and a cannabinoid. The composition may also comprise an exogenous terpene. The cannabinoid is capable of diffusing from the composition into the bloodstream of the user, and may be used in methods for treating a patient suffering from a condition such as pain, nausea and emesis, convulsions, muscle spasm, inflammation, depression, and cachexia.
• US9375417B2
• UNITED STATES OF AMERICA

• Claims:
• 1. A transdermal composition comprising a pharmaceutically effective amount of a cannabinoid for delivery of the cannabinoid to the bloodstream of a user, said composition comprising:
   a) a surfactant-lecithin organogel;
   b) at least one cannabinoid; wherein the cannabinoid is capable of diffusing from the composition into the bloodstream of the user.
• 2. The composition of claim 1, wherein the surfactant-lecithin organogel is present in an amount of between about between about 95% and about 98% w/w.
Cannabinoid patch and method for cannabis transdermal delivery

- US6113940A
- UNITED STATES OF AMERICA

Abstract

- A transdermal structure is provided for delivering cannabis chemical(s) to one's bloodstream. The structure comprises a backing layer which carries the cannabis chemical(s). The chemicals are contained in a film on the backing layer or within a cavity formed in the backing layer. Alternatively, an opening in a secondary layer that overlies the backing layer may be used to create the cavity. The structure is applied to one's skin so that the cannabis chemicals are in contact with the skin. A polymer material which is mixed with the cannabis and placed in the cavity or a membrane over the cavity may be used to control the flow of cannabis chemical(s) into the bloodstream. In an alternative embodiment, a porous material impregnated with cannabis chemical(s) may be used to hold the chemical(s) in the cavity.

https://patents.google.com/
Cannabinoid patch and method for cannabis transdermal delivery

- US6113940A
- UNITED STATES OF AMERICA

Claims

1. A method of delivering cannabis to the bloodstream of a person comprising the steps of:
   A. Providing a transdermal preparation containing cannabis;
   B. Providing a backing layer selected from the group consisting of a patch, strip, bandage and covering for holding said transdermal preparation;
   C. Placing an effective amount of said transdermal preparation onto said backing layer; and,
   D. Attaching said backing layer to the skin of said person so that said transdermal preparation is in contact with said skin.

https://patents.google.com/
Cannabinoid patch and method for cannabis transdermal delivery

- **US6113940A**
- **UNITED STATES OF AMERICA**
- **Claims**
  - 2. The method of claim 1 wherein step A comprises combining said cannabis with a transdermal carrier.
  - 3. A transdermal structure containing cannabis comprising a backing layer selected from the group consisting of a patch, strip, bandage or covering having a reservoir means for holding a transdermal cannabis preparation; and,
  - a transdermal preparation contained in said reservoir means.
Cannabinoid patch and method for cannabis transdermal delivery

https://patents.google.com/
GW Pharmaceuticals Violates Thai Law By Filing 6 Cannabis Patents In Thailand

Department of Intellectual Property: Thailand Patent Search

https://theworldnews.net/th-news/aibo-aithyephykmthraphysinthangpayaakhyabaelw-ykelikkhamkh-sitthibatkaycha-ecchaapayhaa
Cannabis Oromucosal Spray: Product of Thailand

http://englishnews.thaipbs.or.th/rangsit-u-wants-unhindered-experiments-marijuana-medical-use/
Cannabis Oil: Product of Thailand

https://www.youtube.com/watch?v=21rrJoU
Question & Answer