Main Active Principle:
Glycyrrhizin (C_{42}H_{62}O_{16}): 3 - 8% in the licorice root
Responsible for its sweetness.
Approx. 250 times as sweet as cane sugar.

Other well-known components:
Flavonoid glycosides, chalcone glycosides and isoflavonoids.
Pharmacological & Physiological Effects

1. Detoxicant effect
2. Anti-ulcerative
3. Anti-inflammatory
4. Decholesterolization
5. Anti-estrogenic
6. Anti-tussive
7. Anti-histaminic
8. Anti-allergic hepatitis
9. Lowering blood sugar
10. Anti-leukemic
11. Anti-tumor
12. Anti-biotic

Review Of The Relevant Literature
Three Main Actions of Licorice

1. Detoxicant effect
   Synergistic effect of glycyrrhizinic acid and methionine to improve the liver function with GOT and GPT.

2. Anti-ulcerative effect
   - Licorice extract: Anti-gastric and Anti-duodenal ulcerative effect
   - Fractions \((F_{M100})\) other than glycyrrhizinic acid: Anti-ulcerative effect
   - Succinic acid ester made from glycyrrhetinic acid (Disodium 3-succinyloxy-Beta-glycyrrhetinate): Therapeutic agent for gastric ulcers

3. Anti-inflammatory effect
   - Glycryyhetinic acid:
     More effective than hydrocortisone for subacute or chronic skin diseases.
   - Hydrocortisone antagonism:
     Mode of action of glycyrrhetinic acid against the physiological actions of hydrocortisone.
Dipotassium Glycyrrhizinate (DPG)

<Features>
- Effective in treating acute and chronic dermatitis supported by many clinical reports both in Japan and abroad in the field of dermatology.
- Milder action, almost without side effects.
- Widely used in cosmetics because of its chemical stability, good solubility and emulsifying properties.
Dipotassium Glycyrrhizinate (DPG)

<Description>
White to faintly yellow crystalline powder, odorless, characteristic sweet taste

<Stability>
Heat: Very stable, but maybe decomposed if heated at over 100 degrees C for a long time.
pH: When mineral acid is added to the aqueous solution of this product and drop pH under 4, the solution gels.

<Solubility>

<table>
<thead>
<tr>
<th>Solvents</th>
<th>20 º</th>
<th></th>
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<tbody>
<tr>
<td>Water</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>50% Ethanol</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Dehydrated ethanol</td>
<td></td>
<td>×</td>
</tr>
<tr>
<td>1,3-Butylene glycol</td>
<td></td>
<td>×</td>
</tr>
<tr>
<td>Propylene glycol</td>
<td></td>
<td>×</td>
</tr>
<tr>
<td>Chloroform</td>
<td></td>
<td>×</td>
</tr>
<tr>
<td>Ether</td>
<td></td>
<td>×</td>
</tr>
</tbody>
</table>

∮: Very soluble
×: Insoluble
Inflammation

- Redness, Edema, Fever, Pain, Dysfunction, etc.

- Activation of Inflammatory Cell
- Vascular Permeability, etc

- Histamine
- Histamine release inhibition

- PLA₂
- Phospholipids

- Lipoxygenase
- Cyclooxygenase
- LTs, PGs

- Inhibition of LTB₄ and PGE₂ production

- Hyaluronidase inhibition

- Degranulation

- Mast Cell
- Ca²⁺
- Hyaluronidase (non-active)
- Hyaluronidase (active)

- Histamine release
- Histamine

- Capillary Vasodilation
- Edema

- Pain, Itchiness, Redness

- Inhibition of LTB₄ and PGE₂ production

- Accelerate granular enzyme release
<Anti-inflammation and Hyaluronidase>

Inhibition of hyaluronidase plays an important role not only in maintaining the hyaluronic acid level in the body but also in anti-inflammatory and antiallergic activities.\(^1\)

This enzyme is activated during inflammation, plays a role in the destruction of the connective tissue matrix, and increases the permeability of inflammatory cells and blood vessels. Hyaluronidase presents in mast cells in activated by the binding of IgE-antigen complex to receptors, and is involved in the release of histamine granules.

So far anti-inflammatory agents such as indomethacin and antiallergic agents such as sodium cromoglicate have been reported as inhibitors of hyaluronidase.

<table>
<thead>
<tr>
<th>Sample</th>
<th>IC(^{50})(µg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DPG</td>
<td>3.4</td>
</tr>
<tr>
<td>Indomethacin</td>
<td>39.0</td>
</tr>
<tr>
<td>Sodium cromoglicate</td>
<td>11.0</td>
</tr>
</tbody>
</table>

DPG was 11 times stronger than indomethacin and 3 times greater than sodium cromoglicate as positive controls.

Inhibitory Effects on Histamine Release

Fig. 1  Effects of glycyrhizin and glycyrrhetinic acid on histamine release from rat mast cells by antigen IgE antibody reaction.

Concentration of antigen (DNP-As) was 100 μg/ml (%HR : 33.3). Each point represents the mean of duplicate. ●—● : glycyrhizin, ○—○ : glycyrrhetinic acid.

DPG:
Inhibition 83.4% --- Conc. at 1mg/mL

DPG:
Inhibition 86.4% --- Conc. at 2mg/mL

Effects on Arachidonic Cascade


DPG:
Significantly inhibited the LTB₄ production

Clinical Study

Application Of Ointment With DPG For Atopic Dermatitis
Journal of New Remedies & Clinics Vol. 12, No.6 (1983)

Institute: Pediatric Department of Tochigi National Hospital
Subject: 38 patients with atopic dermatitis (M: 17, F: 21)
Test sample: Ointment with 1% DPG
Application: Twice daily
Evaluation: Objective symptom of skin rash,
Subjective symptom of itching

Result: In this clinical study, at least more than 15 days continuous application of the DPG-ointment is recommended.

<table>
<thead>
<tr>
<th>Number</th>
<th>Effective %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Significantly effective</td>
<td>6</td>
</tr>
<tr>
<td>Effective</td>
<td>16</td>
</tr>
<tr>
<td>No effect</td>
<td>16</td>
</tr>
</tbody>
</table>

Among 22 patients with effectiveness:
15 patients- - - More than 15 days application
7 patients- - - Less than 15 days application