

DI POTASSIUM GLYCYRRHIZINATE



 MARUZEN PHARMACEUTICALS CO., LTD.

Components Of Licorice

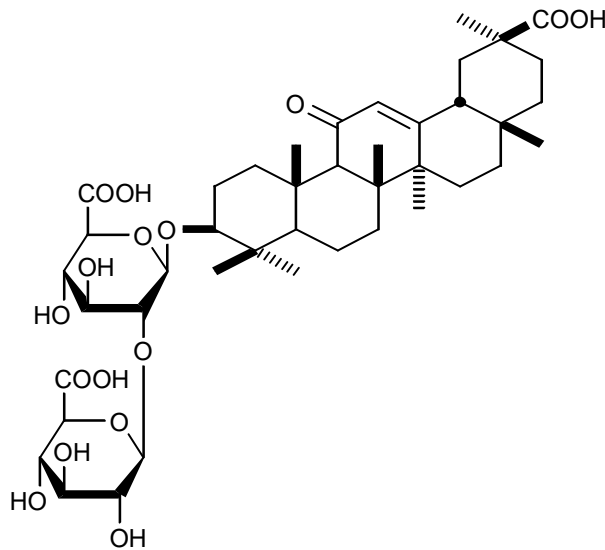
Main Active Principle:

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.

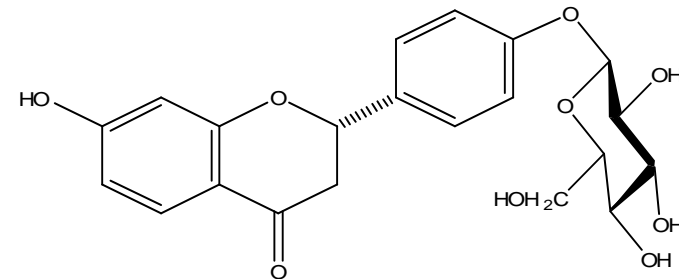


Other well-known components:

Flavonoid glycosides, chalcone glycosides and isoflavonoids.



Glycyrrhizin



Liquiritin

Review Of The Relevant Literature

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.

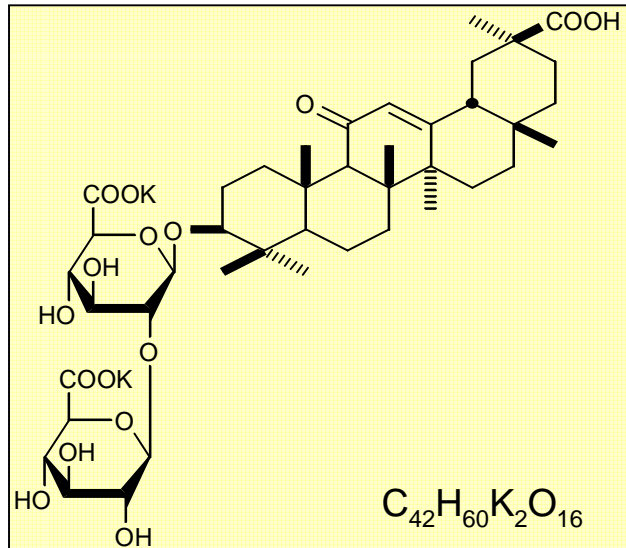
2. Anti-ulcerative effect

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

3. Anti-inflammatory effect

- Glycyrrhetic acid:
More effective than hydrocortisone for subacute or chronic skin diseases.
- Hydrocortisone antagonism:
Mode of action of glycyrrhetic 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.
- An “anti-inflammatory” active constituent in Quasi-Drug in Japan.

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.

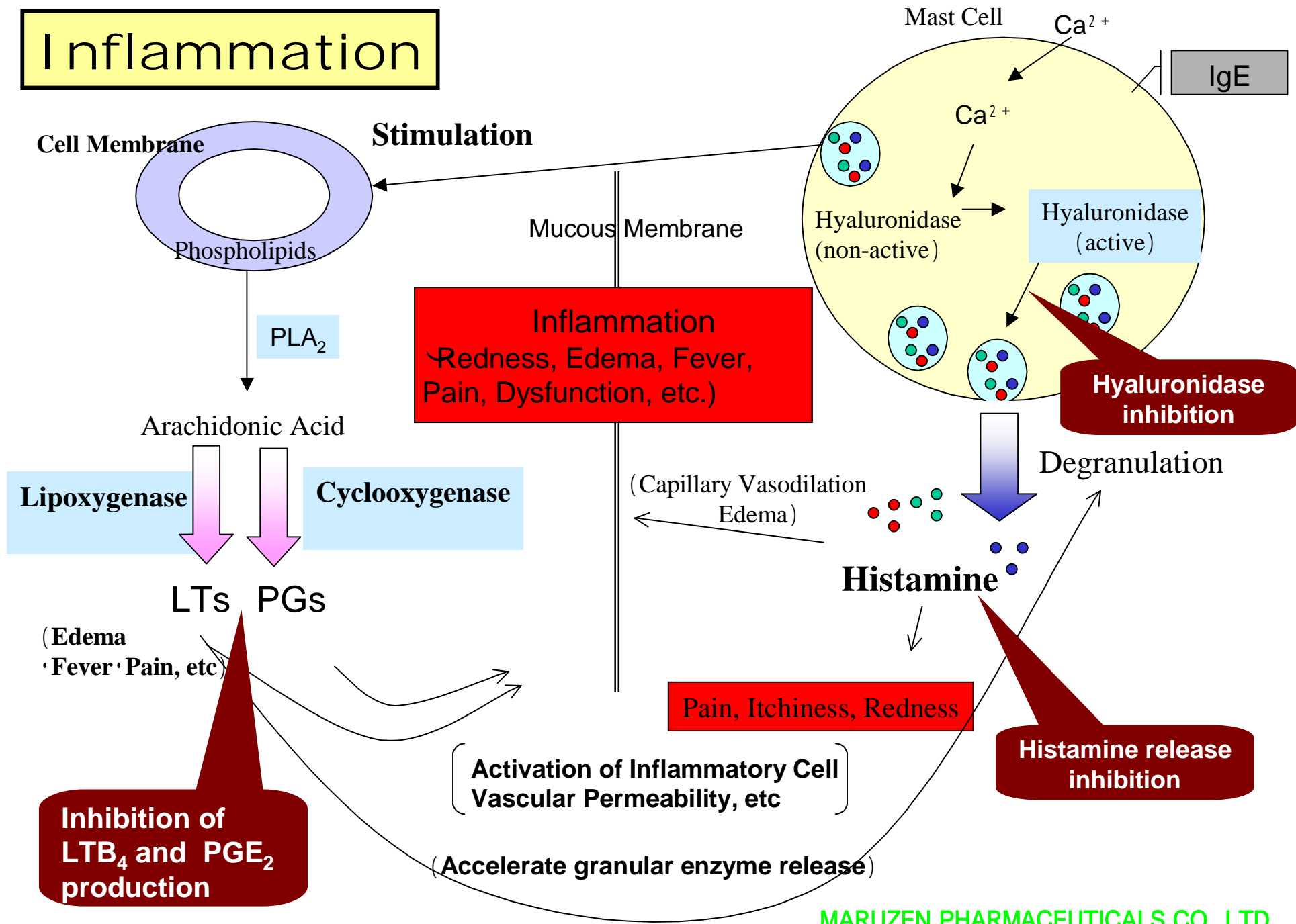
pH: When mineral acid is added to the aqueous solution of this product and drop pH under 4, the solution gels.

<Solubility>

Solvents	20
Water	
50%Ethanol	
Dehydrated ethanol	×
1,3-Butylene glycol	×
Propylene glycol	×
Chloroform	×
Ether	×

: Very soluble
×: Insoluble

Inflammation



Inhibitory Effect on Hyaluronidase Activity

<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⁾

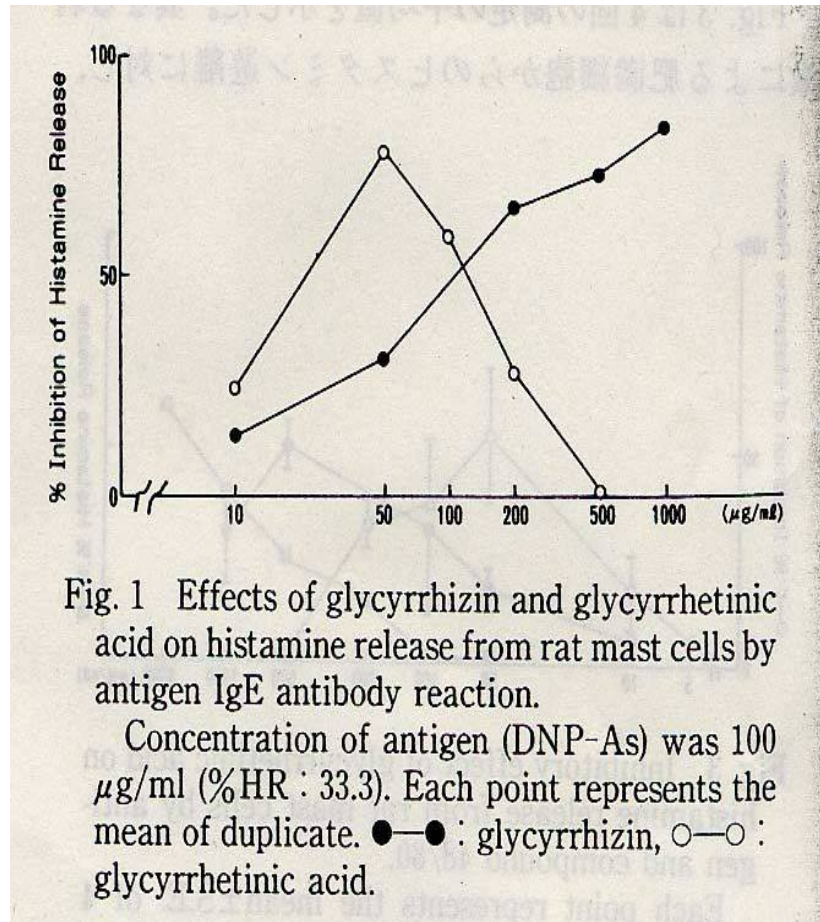
This enzyme is activated during inflammation, plays a role in the destruction of the connective tissue matrix, and increases the permeability of inflammatory cells and blood vessels. Hyaluronidase presents in mast cells in activated by the binding of IgE-antigen complex to receptors, and is involved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

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

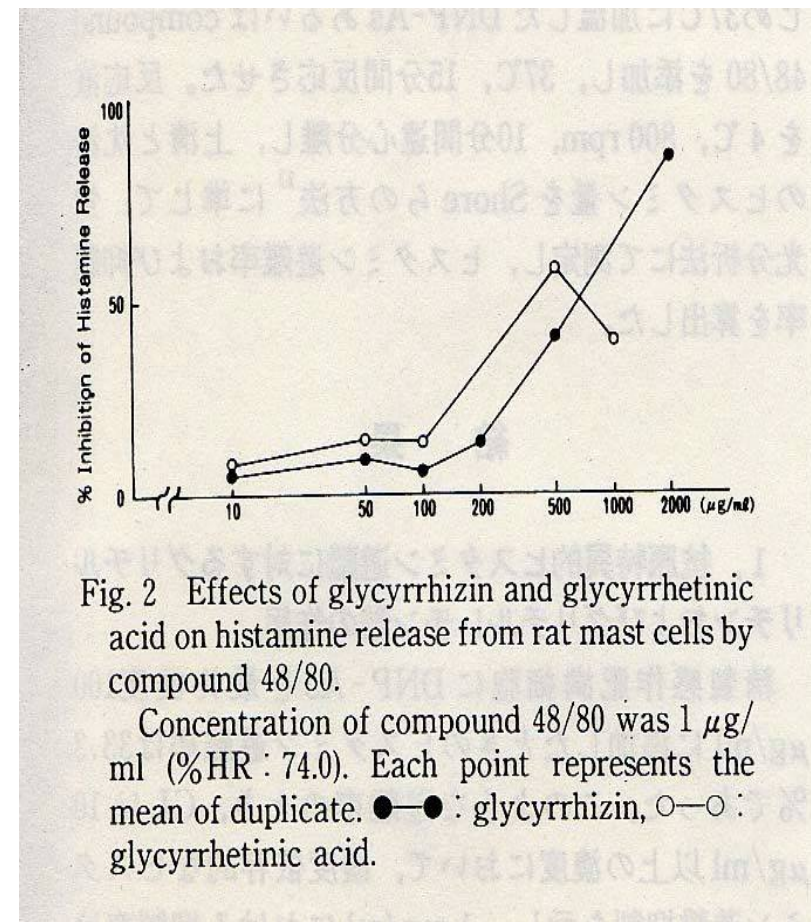
Sample	IC ₅₀ (μ g/mL)
DPG	3.4
Indomethacin	39.0
Sodium cromoglicate	11.0

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

Inhibitory Effects on Histamine Release



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



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

Ref: Tadayoshi Shibata, Journal of WakanMedical and Pharmaceutical Society
for WAKAN-YAKU 6, 294 (1989)

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Effects on Arachidonic Cascade

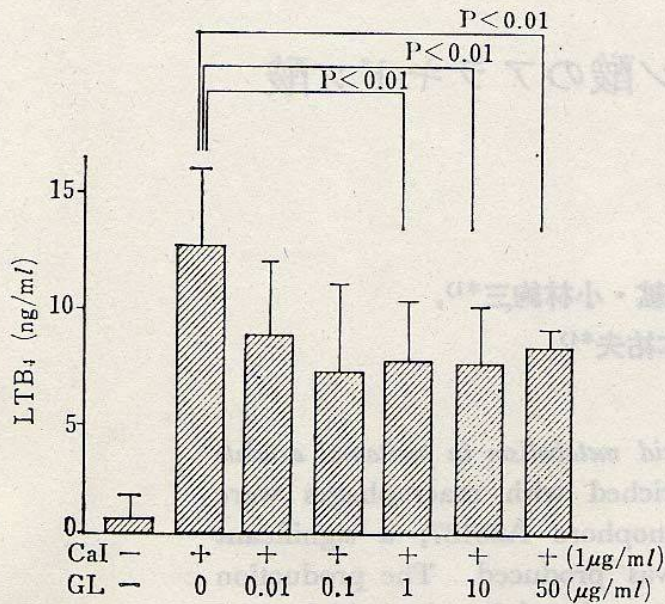


図 1 effect of glycyrrhizin on LT B₄ production by rat peritoneal exudate cells stimulated with calcium ionophore A23187 (CaI)

All value are mean ± standard error of 7 experiments.

DPG:
Significantly inhibited the LTB₄ production

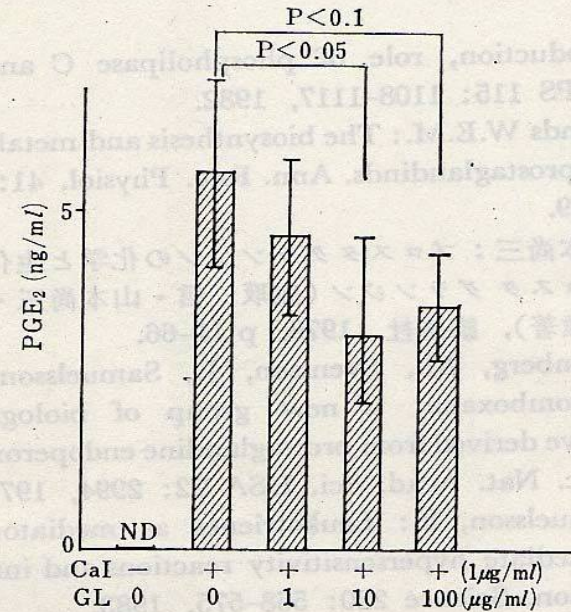


図 4 effect of glycyrrhizin on PGE₂ production by rat peritoneal exudate cells stimulated with calcium ionophore A23187

All value are mean ± standard error of 7 experiments.

DPG:
Significantly inhibited PGE₂ production

Ref: Norifumi Kawada, Inflammation 9(1), 29 (1989)

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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.

	Number	Effective %
Significantly effective	6	57.9%
Effective	16	
No effect	16	42.1%

Among **22** patients with effectiveness:

15 patients - - More than 15 days application

7 patients - - - Less than 15 days application