Development of Gel Formulation of Merremia mammosa (Lour.) Water Fraction as a Topical Drug on Diabetic Wound Healing Treatment

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DEVELOPMENT OF GEL FORMULATION OF *MERREMIA MAMMOSA (LOUR.)* WATER FRACTION AS A TOPICAL DRUG ON DIABETIC WOUND HEALING TREATMENT

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[Background]

Treatment of diabetic ulcer is quite difficult, because of the defective of blood vessels and bacterial infection. Water fraction of *Merremia mammosa (Lour.)* extract that contains flavonoids proven to have potential antioxidant activity that helps the wound healing process in our previous study. Therefore, it is potential to be developed further as a topical drug for the prevention of diabetic ulcer.

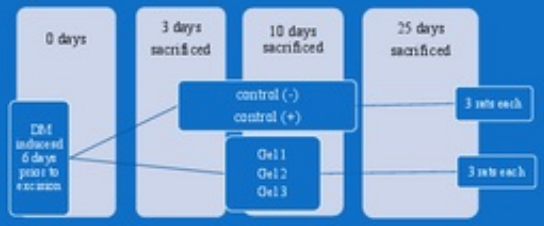
This study aims to develop gel formulation of *Merremia mammosa (Lour.)* water fraction and searching the most potent gelling agent in wound healing treatment of diabetic rat model.

[Materials and Methods]

This experimental study used forty-five male Wistar rats that were made diabetic by intraperitoneal injection of 40 mg/kg b.w. weight streptozotocin. Rats divided into five groups, which consist of negative control (aquadest), positive control (bioplacento), and 10% of the water fraction of *Merremia mammosa (Lour.)* extract in each 1.5% base (HPMC, Carbopol, CMC Na).

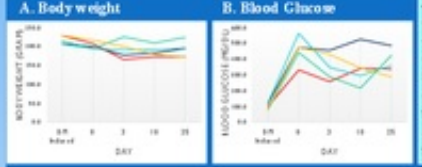
Wound was made by Morton method and treatment applied on the wound every other day for 25 days. Wound healing process were observed by calculating the percentage of reduction in wound size. Histopathology parameter also being observed at day 3, 10 and 25 following wound healing phase. Safety test were done in rabbits with OECD guideline 404. Data were described and analyzed further using appropriate statistic tools.

Morton method excision on wistar rats weight 150-250 g



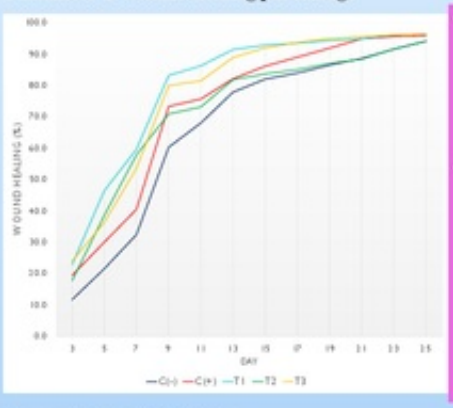
[Results and Discussions]

A. Body weight **B. Blood Glucose**



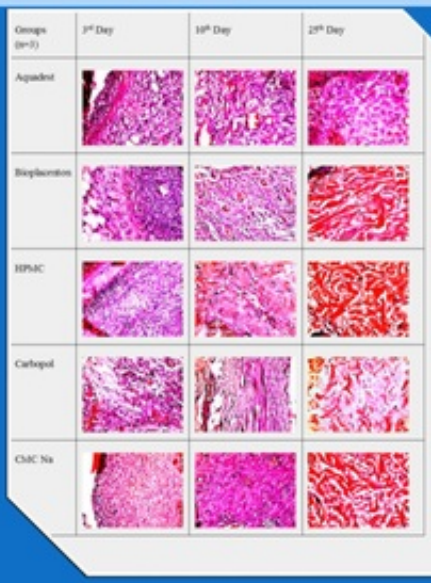
A. Body weight in all groups showed a slight decrease and then gradually increase.
B. All non-fasting blood glucose was higher than 200 mg/dL in the entire experimental time.

Parameter 1: Wound healing percentage



- The percentage of reduction in wound size comparison showed a different in every gelling agent when compared with negative control, although not statistically significant.
- This study showed that among the three gelling agents, HPMC and CMC Na had similar healing rate in relevant with the high bioavailability and Carbopol was the less. This result proved that different gelling agent provides different release rate that may affect the drug potency.

Parameter 2 : HE staining



Photomicrograph observation in each healing phase showed
- There were no different yet on day 3 of wound excision.
- While on day 10 and 25 showed that only Carbopol had slower wound healing rate compared to other gelling agents by evaluating the amount of angiogenesis, macrophage, fibroblast and collagen, relevant with macroscopic appearance.
- Other gelling agents were similar to bioplacenton (positive control) healing phase, described by optimum number of collagen and none of macrophage.

Parameter 3 : Safety test

The wound irritation test to see the safety of the gel showed only the rabbit applied with the Na CMC gelling agent that did not experience any erythema or edema during the test.

Gelling agent	1st hour		24th hour		48th hour		72nd hour	
	Edema	Erythema	Edema	Erythema	Edema	Erythema	Edema	Erythema
HPMC	-	-	-	1st degree	-	1st degree	-	-
Carbopol	-	1st degree	-	1st degree	-	1st degree	-	-
CMC Na	-	-	-	-	-	-	-	-

The further experiment will examine whether these results supported by
1) MTT staining for specific histopathology collagen parameter
2) Hydroxyproline for specific biochemistry collagen parameter
3) VEGF for specific immunohistochemistry angiogenesis parameter

[Conclusions]

① Gel formulation of *Merremia mammosa (Lour.)* water fraction accelerated the process of wound healing in diabetic rat model.
② The safest and suggested gelling agent to be developed as a topical drug was CMC Na.

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