Development of an Antiflatulent Topical Gel from Ya-Tha-Thong-Sut-Nueng, a Thai Herbal Preparation for Flatulence

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Abstract. This study focused on the development of an antiflatulent topical gel from a Thai herbal preparation "Ya-Tha-Thong-Sut-Nueng". This herbal formula comes in powder form and needs to be prepared with alcohol before being applied topically. Because of this, using it in daily life is inconvenient. Thus, the development of its topical gel was carried out. The gel formulations, of which the ingredients contained Carbopol 940, triethanolamine, glycerine, propylene glycol, ethanol, purified water, and the extract of Ya-Tha-Thong-Sut-Nueng, were investigated in 6 different formulae. The developed gel was evaluated for physical properties (texture, color, odor, viscosity, spreadability, and stain after application) and chemical properties (pH) under accelerated conditions of a heating-cooling cycle. The finest physical and chemical characteristics were discovered in gel formula no. 1 consisting of 1.0 g of the extract, 0.4 g of Carbopol 940, 0.17 g of triethanolamine, 1.0 g of glycerine, 4.0 g of propylene glycol, 10.0 g of ethanol, and 83.43 g of purified water. Moreover, the gel had a smooth appearance without any indications of separation or precipitation, and it was viscous, turbid, and light brown semi-solid. Additionally, it provided a decent spreadability across the skin after topical application without leaving any residue behind. The gel had a viscosity of 9,564.5 ± 250.7 cP, while its pH was 5.63 ± 0.01 which was according to the chemical property criteria of Thai Industry Standard 478-2555. The developed gel formula no. 1 was easy to use and portable. However, additional research on the stability of the bioactive components in the formula under accelerated settings should be done to guarantee the stability of the gel.

Keywords: Thai herbal preparation; Ya-Tha-Thong-Sut-Nueng; topical gel; flatulence.

1. Introduction

Normal individuals of all ages have frequently experience of flatulence. Food overconsumption, gas-producing foods and beverages, constipation, and other conditions can be all causes of the symptom [1]. The conventional treatment for flatulence involves using over-the-counter medications like sodamint tablets, magnesium hydroxide-aluminum hydroxide-simethicone solution, and aluminum hydroxide tablets [2]. Prolonged use of these medicines leads to constipation, an increase in food allergy, and diarrhea in some cases. According to Thai traditional medicine knowledge, it has long employed several herbal drug formulations to

eliminate excess gas. Ya-That-Ban-Job, Ya-That-Ob-Choei, Ya-Tha-Thong-Sut-Neung are those antiflatulent medications. The National Thai Traditional Medicine Formulary's Ya-Tha-Thong-Sut-Neung, which was also known as a Thai topical herbal formula 1, comprises one part of each herb, including garlic, ginger, winged bean root, black pepper, shallot, mahahing, and sea salt (Table 1) [3]. It's utilized for indigestion and gas relief in a powder form that must be mixed with alcohol before applying topically. It is therefore inconvenient to utilize in daily life. This, together with no reports on the development of Ya-Tha-Thong-Sut-Neung in various dosage forms, prompted us to develop it as a topical gel.

Table 1 The herbal ingredients of Ya-Tha-Thong-Sut-Nueng

Herbal ingredient	Scientific name	Part used
1) Garlic	*Allium sativum* L.	Bulb
2) Ginger	*Zingiber officinale* Roscoe	Rhizome
3) Winged bean	*Psophocarpus tetragonolobus* (L.) DC.	Root
4) Black pepper	*Piper nigrum* L.	Fruit
5) Shallot	*Allium ascalonicum* L.	Bulb
6) Mahahing	*Ferula assa-foetida* L., *F. foetida* (Bunge) Regel	Root latex
7) Sea salt	Sodium chloride	-

2. Materials and Methods

2.1. Herbal materials

Dried herbal plants (garlic, ginger, black pepper, and mahahing) and sea salt were purchased from Charoensuk Pharma Supply Co., Ltd. in Nakhon Pathom province in May 2020, while dried winged bean root was obtained from Rungrueang Osot in Phichit province. Fresh shallot procured from Makro department store at Rangsit in Pathum Thani province was thoroughly cleaned, sliced into small pieces, and dried in a hot air oven at 50 ^{o}C for 12 hours. All the dried plants were then separately ground using an electric grinder and passed through a sieve no. 60. The powdered drugs contained in a zip bag were kept in a desiccator prior to use. Based on Thai traditional medicine, sea salt and mahahing require pre-preparation before being subjected to compounding of traditional medicinal preparation as follows; to a clay pot, sea salt was added and heated until it became dry and fluffy. This process was done to dry and clean the salt. For mahahing, it was pounded into small pieces and dissolved with boiling water of red holy basil leaves. The resulting solution was passed through a cotton gauze filter cloth and dried in a hot air oven at 30 ^{o}C for 12 hours [3].

2.2. Chemicals

Carbopol 940, triethanolamine (TEA), glycerine, propylene glycol (PPG), and ethanol (95%), all of which were cosmetic grade, were purchased from Hong Huat Co., Ltd. in Pathum Thani province. Commercial-grade ethanol (95%) used for the herbal extraction was procured from CT Laboratory Co., Ltd. in Bangkok.

2.3. Preparation of the herbal extract

One portion of each powdered herbal ingredient was combined and macerated thrice with 95% ethanol for 5 days each; the herbal materials to solvent ratio was 1:1 (w/v). Filtration through a Whatman filter paper no. 1 gave a filtrate. The pooled filtrate was evaporated in vacuo to dryness, and the obtained extract was kept in a desiccator.

2.4. Gel formulation

Six distinct formulae were used to formulate the gel, each derived from an alcohol-based gel formulation with the compositions listed in Table 2 [4]. Carbopol 940 was first dispersed in water and left to complete dispersion. The extract was dissolved in 95% ethanol. After that, glycerine and PPG were added to the ethanolic extract and mixed well. The obtained mixture was then added to the completely dispersed Carbopol 940 and mixed well. Finally, TEA was added to the gel to reach a pH between 6-7.

Table 2 The compositions of the gel base

Ingredient	Amount (g)	Function
1) Carbopol 940	0.5	Gelling agent
2) TEA	q.s. pH 6-7	pH adjuster
3) Glycerine	5	Humectant
4) PPG	5	Humectant
5) Ethanol	52	Co-solvent
6) Purified water	q.s. to 100	Co-solvent

2.5. Physicochemical properties

The physical and chemical properties of the developed gels were assessed. Organoleptic observation was performed by examining changes in texture, color, odor, spreadability, and staining following application. Additionally, the same author conducted sensory tests of texture, spreadability, and stain on the inside surface of the forearm [5]. The spreadability is the degree to which a product is easily applied to the skin [6]. pH values in triplicate were determined using a calibrated Sartorius PB-10 pH meter at room temperature. Viscosity was measured in triplicate by a Fungilab Visco Star plus rotating viscometer along with a stainless-steel spindle no. L4 at room temperature. Results were expressed in centipoise (cP).

2.6. Stability study

The developed gel contained in a clear PET pump bottle was subjected to an accelerated setting using a heating-cooling procedure in a Binder KBF 240 climatic chamber with a relative humidity of 75%. Six cycles of heating and cooling were performed. Each cycle consisted of 48 hours of storage at 4°C followed by 48 hours of storage at 45°C. The physicochemical parameters of the gel were determined during the 0^{th}, 3^{rd}, and 6^{th} cycles.

2.7. Statistical analysis

Data were expressed as mean±SD of three determinations calculated by the Microsoft Excel program. Statistical analysis was performed by a one-way analysis of variance (ANOVA), and differences were regarded as significant at the level of $p < 0.05$.

3. Results and Discussion

3.1. Gel formulation

The development of gel from the extract of Ya-Tha-Thong-Sut-Neung (Figure 1) was carried out by varying the amount of the gel compositions. After determining the appropriate quantities for each of the gel's components, the final amounts were displayed in Table 3. The amounts of the extract were in a range of 1-6 g which led to 6 different gel formulae.

Table 3 The compositions of six investigated gel formulae

Formula no.	Ingredients (g)						
	Crude extract	Carbopol 940	TEA	Glycerine	PPG	Ethanol	Purified water
1	1.0	0.4	0.17	1.0	4.0	10.0	83.43
2	2.0	0.4	0.17	1.0	4.0	10.0	82.43
3	3.0	0.4	0.17	1.0	4.0	10.0	81.43
4	4.0	0.4	0.17	1.0	4.0	10.0	80.43
5	5.0	0.4	0.17	1.0	4.0	10.0	79.43
6	6.0	0.4	0.17	1.0	4.0	10.0	78.43

3.2. Physicochemical properties

The freshly prepared gels had a physical appearance as displayed in Figure 2 (0th cycle). All the gels displayed uniformity and smoothness, accompanied by a distinct scent of organosulfur compounds, which are one of the primary chemicals found in mahahing [7]. It exhibited that the pH of all the gels was in a range of 5.62-5.94, which was in agreement with Thai Industry Standard 478-2555 (TIS 478-2555) [8]. As the amount of the extract increased, their viscosity dropped, ranging from 9,564.5 to 3,515.0 cP. This behavior would result from the salting out effect, which is the competitive interaction of sodium ions in sea salts with water molecules, reducing the contact between the water and the gelling agent (Carbopol 940). On the one hand, the decreased viscosity should be caused by the sodium ions' own electrostatic repulsion [9]. Moreover, increased quantities of sodium ions in gels increase the likelihood of precipitation.

Figure 1 The physical appearance of the extract from Ya-Tha-Thong-Sut-Neung

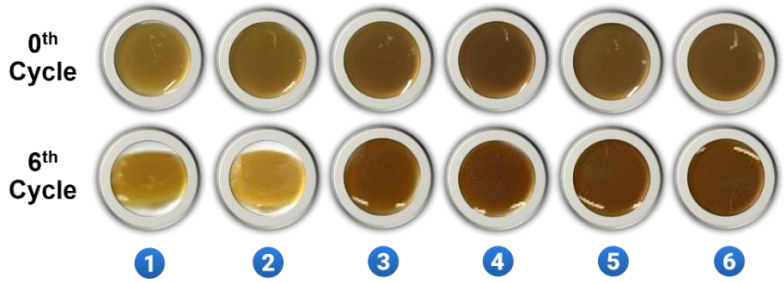

Figure 2 The physical appearance of the gels obtained under accelerated conditions

3.3. Stability study

All the gels were tested for stability under accelerated settings using a heating-cooling cycle technique. Figure 2 depicts the gel's physical appearance after the 6th round of stability testing. Following the completion of the 6th cycle, the color of the gel formula no. 4 increased (Figure 2, Table 4). Moreover, it produced a stain on the skin after topical treatment.

Table 4 The gels' physicochemical properties from the 6th cycle of a heating-cooling cycle

No.	Physical properties						pH
	Texture after application	Color	Odor	Viscosity (cP)	Spreadability	Stain after application	
1	Not watery, smooth, nonsticky	Turbid light brown	Pungent	9,280.8±8.0	+++	ND	5.63±0.01
2	Not watery, smooth, nonsticky	Turbid light brown	Pungent	5,659.1±48.9	+++	ND	5.65±0.01
3	Watery, smooth, sticky	Turbid dark brown	Pungent	3,774.8±11.4	++	ND	5.63±0.01
4	Watery, smooth, sticky	Turbid dark brown	Pungent	3,440.1±41.2	++	Brown stain	5.95±0.01
5	Watery, smooth, sticky	Turbid dark brown	Pungent	3,469.1±85.6	++	Brown stain	5.66±0.01
6	Watery, smooth, sticky	Turbid dark brown	Pungent	3,379.0±144.8	++	Dark brown stain	5.67±0.01

+++ = good spreadability, ++ moderate spreadability, + = poor spreadability, ND = not detected

The gel formulation nos. 5 and 6 showed the same outcomes. Of all the gels, their pH shifted slightly (Table 5), whereas their viscosity decreased throughout the stability test. This was caused by the instability of polyacrylic acid polymers in the presence of electrolytes as well as the polymer's tendency to break down at elevated temperatures. As a result, the viscosity decreased [10]. However, there was no statistically significant difference in the viscosity of the gels between the 0th and 6th cycles (Table 6). This demonstrated the developed gels' stability.

Table 5 The pH of the gels measured at the 0th, 3rd, and 6th cycles

Formula no.	pH		
	0th cycle	3rd cycle	6th cycle
1	5.63±0.01	5.64±0.01	5.63±0.01
2	5.65±0.01	5.65±0.01	5.65±0.01
3	5.62±0.01	5.63±0.01	5.63±0.01
4	5.95±0.02	5.94±0.01	5.95±0.01
5	5.66±0.01	5.66±0.01	5.66±0.01
6	5.67±0.01	5.67±0.01	5.67±0.01

Table 6 The viscosity of the gels measured at the 0th, 3rd, and 6th cycles

Formula no.	Viscosity (cP)			*P*-value	R
	0th cycle	3rd cycle	6th cycle	(0th and 6th cycles)	(average)
1	9,564.5±250.7	9,370.9±10.9	9,280.8±8.0	0.442	283.7
2	5,903.5±113.8	5,794.2±20.3	5,659.1±48.9	0.740	244.4
3	3,987.6±26.1	3,995.5±40.3	3,774.8±11.4	0.438	212.8
4	3,446.8±39.9	3,512.7±33.1	3,440.1±41.2	0.155	6.7
5	3,540.6±31.6	3,603.0±20.3	3,469.1±85.6	0.372	71.4
6	3,515.0±14.9	3,647.6±77.2	3,379.0±144.8	0.117	136.0

$p < 0.01$ = the treatment means are highly significantly different.
$0.01 < p < 0.05$ = the treatment means are significantly different.
$p > 0.05$ = the treatment means are not statistically significantly different.
R = the range of data which is the difference between the 0th-cycle and 6th-cycle viscosities

According to the investigation, the gel formulation no. 1 had the most stable physicochemical characteristics. The gel had a smooth texture without any indications of separation or precipitation, and it was nonsticky, turbid, and light brown semi-solid. Additionally, it provided

a decent spreadability across the skin after topical application without leaving any residue behind. The gel had a viscosity of 9,564.5 ± 250.7 cP, while its pH was 5.63 ± 0.01 which was according to the chemical property criteria of TIS 478-2555. Additionally, the gel formulation no. 2 had the same physicochemical properties as the gel formulation no. 1, but a lower viscosity. The reduced viscosity of the gel would be caused by the larger extract amount in the formulation [9]; this could lead to gel precipitation and poor performance upon long-term storage.

This study reported on the first topical gel formulation of Ya-Tha-Thong-Sut-Neung. It would be interesting to see this herbal product developed in additional dosage forms. Nevertheless, more research on the stability of active chemicals in the gel is needed to confirm the developed gel's stability, as well as an investigation of the gel's drug release profile. Furthermore, heavy metal and microbiological contaminations should be performed following TIS 478-2555.

4. Conclusion

Gel formulations containing Carbopol 940, TEA, glycerine, PPG, ethanol, purified water, and Ya-Tha-Thong-Sut-Neung extract were examined in six different formulae. The developed gel was evaluated for its physical properties (texture, color, odor, viscosity, spreadability, and stain after topical application) and chemical properties (pH) under accelerated conditions using a heating-cooling procedure. The gel formula no. 1 had the best physical and chemical properties, containing 1.0 g of extract, 0.4 g of Carbopol 940, 0.17 g of TEA, 1.0 g of glycerine, 4.0 g of PPG, 10.0 g of ethanol, and 83.43 g of purified water. The gel exhibited a smooth texture with no signs of separation or precipitation; it was nonsticky, turbid, and pale brown semi-solid. Furthermore, it produced a good dispersion across the skin upon topical application without leaving any residue. The gel had a viscosity of $9{,}564.5 \pm 250.7$ cP, while its pH was 5.63 ± 0.01 which was according to the chemical property criteria of Thai Industry Standard 478-2555. The developed gel formula no. 1 was easy to use and portable. However, additional research on the stability of the bioactive components in the formula under accelerated settings should be done to guarantee the stability of the gel.

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