

Formulation Development and In Vitro Antacid Activity of Herbal Effervescent Granules

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Abstract: *The antacids act by neutralizing the acid in the stomach and by inhibiting pepsin, which is a proteolytic enzyme. Each of these cationic salts has a characteristic pharmacological property that determines its clinical use. In recent years, demands of identification and evaluation of new drugs possibly of plant origin are gaining popularity for the treatment of various gastrointestinal diseases. Hence, herbal medicines were considered a better substitute for the treatment of acid reflux/ acidity with lesser adverse side effects. The main objective of the study was to select herbs which were used as a home - remedy, having properties for neutralizing the acid of the stomach viz Cumin (*Cuminumcyminum*), Sprague (*Trachyspermumammi*), and Peppermint (*Menthapiperita*) and incorporate in their extract forms individually into the novel formulation (Effervescent granules) developed by using wet granulation method. Also, a formulation was developed by mixing extracts of Sprague and peppermint. The formulations developed were evaluated for flow properties, effervescence cessation time, and antacid properties. The antacid activity was determined using preliminary antacid test, acid neutralization potential, and acid neutralization capacity. The study proves the efficiency of the herbs used as an API in treating acidity. Along with the antacid activity, these herbs help to improve the secretion of enzymes and digestion in the gut.*

Keywords: antacid, effervescent, acidity, Aurvedic, herbal

1. Introduction

Acidity, also called acid reflux, may be a condition that's characterised by heartburn that's felt round the lower chest area. ¹ It is a standard condition that happens when stomach acid flows into the food pipe. The most common acid reflux symptom is a burning sensation in the chest, and pain. ² Based on the condition and the depth of the acid reflux problem, prescription of an antacid that contains aluminium, calcium or magnesium may be given. ³ The antacids act by neutralizing the acid in the stomach and by inhibiting pepsin, which is a proteolytic enzyme. ⁴ They are designed to dissolve in water, and then release a level of carbon dioxide. ⁴ The common ingredients are acid and bicarbonate of soda, which react when in touch with water to supply CO₂. ⁴ Effervescent antacids may also contain aspirin, sodium bicarbonate, or tartaric acid. ⁴ The most preferred and sold antacid formulations are effervescent antacid tablet/granules. ¹ They are known for their quick action and relief which ultimately makes them the most desired line of treatment for acidity. Three naturally available herbs, Cumin (*Cuminumcyminum*), Sprague (*Trachyspermumammi*), and Peppermint (*Menthapiperita*) were selected based on their properties.

Cumin (*Cuminumcyminum*): In the traditional therapies, cumin seeds are prominently considered carminative, eupeptic, antispasmodic, astringent and used in the treatment of mild digestive disorders, diarrhoea, dyspepsia, flatulence, morning sickness, colic, dyspeptic headache and bloating, and are said to promote the assimilation of other herbs and to improve liver function. ⁵ The alcoholic extract of cumin shows anti - spasmodic effect viz inhibitory effects on

smooth muscle contractions induced by the spasmogen, acetylcholine and histamine. ⁶

Sprague (*Trachyspermumammi*): Traditional practitioners recommend the herb as a digestive stimulant medicine. Sprague increases the secretion of gastric acid, bile acids and activity of digestive enzymes. It also reduces the food transient time. ⁷ As the enzyme modulatory activity, sprague reinforces the pancreatic lipase and amylase effectiveness, which supports the digestive stimulant activity. ⁷

Peppermint (*Menthapiperita*): Peppermint is one of the oldest and most highly regarded herbs for appeasing digestion and may also restore digestive efficiency. In addition, peppermint has been known as disorders improving including: analgesic, ulcer, anti - spasmodic, anti - bloat, irritable bowel syndrome or gastrointestinal motility, and immune system stimulant and etc. ⁸ Peppermint essential oil (menthol) has biological activities, such as antibacterial, antifungal and antioxidant properties. ⁸

Keeping in mind the knowledge of naturally available herbs and most commonly used home remedies for acidity, this research aims at formulating and evaluating the herbal effervescent antacid granules prepared by incorporation of herbs as active pharmaceutical ingredients (API).

2. Methods

1) Formulation

Three different formulations were formulated to check the best formulation for the preparation of herbal effervescent granules. In these 3 formulations, different ingredients and different concentrations of the excipients viz. effervescing mixture, sodium bicarbonate, binder and lubricants were

used. After selection of the best out of these three formulations, four different types of herbal products were prepared using sprague, cumin and peppermint. 100 g of effervescent granules were prepared using the formulations given in the Table 01. These formulations were prepared using simple wet granulation technique.

Table 1

Ingredients	Formulation 1 (F1)	Formulation 2 (F2)	Formulation 3 (F3)
Antacid	Sodium Bicarbonate 24g	Sodium Bicarbonate 44g	Sodium Bicarbonate 44g
Effervescing Agent	Tartaric Acid 20g	Tartaric Acid 20g	Tartaric Acid 25g
Effervescing Agent	Citric Acid 17g	Citric Acid 17g	Citric Acid 12.5g
Sweetener	Aspartame 12g	Saccharin 12g	Saccharin 11.4g
Diluent	Lactose 20g	-	-
Binder 1	Sodium CMC 2g	PEG 2g	PVP K30 3.75g
Binder 2	Starch paste 5%	PVP in ethanol 10%	Starch paste 5%
Lubricant	Magnesium Stearate 0.5%	Magnesium Stearate 0.5%	Magnesium Stearate 0.5%
Glidant	Talc 1%	Talc 1%	Talc 1%

All the ingredients were weighed and passed via sieve no.20 to get free flowing powder.

The powders were geometrically mixed. Binders were added as required and a granulating mixture was prepared. The mixture was passed through sieve no.20 and the granules were collected. These granules were dried in oven at 60°C for 75 minutes. The dried granules were passed through sieve no.40 and retained on sieve no.60. Lubricant and glidant were later added.

2) Evaluations of Granules

Table 2

Test	Formulation 1 (F1)	Formulation 2 (F2)	Formulation 3 (F3)
Angle of Repose	30°	26.1	22.3°
Bulk Density	0.66	0.68	0.78
Tap Density	0.78	0.78	0.86
Carr's Index	0.18	0.12	0.0903
% Compressibility	18%	12%	9.03%
Hausner's Ratio	0.88	0.871	0.906
Effervescent cessation time	361 sec	501 sec	625 sec

Table 3

Ingredients	Formulation 4 (F4)	Formulation 5 (F5)	Formulation 6 (F6)	Formulation 7 (F7)
Antacid	Sodium Bicarbonate 44g	Sodium Bicarbonate 44g	Sodium Bicarbonate 44g	Sodium Bicarbonate 44g
Effervescing Agent	Tartaric Acid 25g	Tartaric Acid 25g	Tartaric Acid 25g	Tartaric Acid 25g
Effervescing Agent	Citric Acid 12.5g	Citric Acid 12.5g	Citric Acid 12.5g	Citric Acid 12.5g
Sweetener	Saccharin	Saccharin	Saccharin	Saccharin

From the results we conclude that Formulation three had the best parameters and flow properties. Hence formulation three was selected as the parent formulation for the preparation of the herbal effervescent granules. Formulation (F3) had the most compliant flow property and the longest effervescent cessation time among the three formulations.

3) Extractions

a) Extraction of Peppermint Leaves (*Menthapiperita L.*)

Peppermint leaves (*Menthapiperita L.*) were collected from H. K. College of Pharmacy. The leaves were washed and 15g of fresh peppermint leaves was weighed. The leaves were crushed and 10 ml of distilled water was added to it. The sludge was warmed and concentrated. The juice was filtered and collected.

b) Extraction of Cumin Seeds (*Cuminumcyminum*)

Cumin seeds (*Cuminumcyminum*) were purchased from a local store of the packing Exotica the world of spice packaged by Exotica International.50 grams of seeds were weighed and powdered.20 ml of water was added and the mixture was boiled. The extract was filtered and collected using a muslin cloth.

c) Extraction of Sprague Leaves (*Trachyspermumammi L.*)

Sprague leaves (*Trachyspermumammi L.*) were collected from H. K. College of Pharmacy. The leaves were washed and 20 g of fresh leaves was weighed. The leaves were crushed and 15 ml of distilled water was added. The sludge was boiled and concentrated. The juice was filtered and collected using a muslin cloth.

4) Preparation of Herbal Effervescent Granules

The ingredients and quantities were selected according to Formulation 3 for the preparation of 100 g of herbal effervescent granules. Four different types of herbal effervescent granules were prepared using the extracts of cumin, sprague and peppermint. All the ingredients were weighed and passed via sieve no.20 to get free flowing powder. The powders were geometrically mixed. The extracts were added along with the binders while formulating the granulating mixture. The granulating mixture was passed through sieve no.20 and granules were dried at 60°C for 75 minutes. The dried granules were further passed through sieve no.40 and retained at sieve no.60.

	11.4g	11.4g	11.4g	11.4g
Binder 1	PVP K30 3.75g	PVP K30 3.75g	PVP K30 3.75g	PVP K30 3.75g
Binder 2	Starch paste 5%	Starch paste 5%	Starch paste 5%	Starch paste 5%
Extract	Cumin Extract 2 ml	Sprague Extract 2 ml	Peppermint Extract 2 ml	Sprague + Peppermint Extract 1 ml each
Lubricant	Magnesium Stearate 0.5%	Magnesium Stearate 0.5%	Magnesium Stearate 0.5%	Magnesium Stearate 0.5%
Glidant	Talc 1%	Talc 1%	Talc 1%	Talc 1%

5) Evaluations of Herbal Effervescent Granules

Table 4

Test	Formulation 4 (F4)	Formulation 5 (F5)	Formulation 6 (F6)	Formulation 7 (F7)
Angle of Repose	21.7	22.5	23	22.4
Bulk Density	0.79	0.80	0.78	0.81
Tap Density	0.87	0.86	0.87	0.90
Carr's Index	0.092	0.069	0.103	0.1
% Compressibility	9.2%	6.9%	10.3%	10%
Hausner's Ratio	1.101	1.075	1.115	1.111
Effervescent cessation time	610 sec	595 sec	625 sec	590 sec

6) Preliminary in - vitro evaluations for antacid activity

Antacids are alkaline substances that reduce gastric acidity by neutralization of hydrochloric acid in the stomach. Moreover, pharmacological properties have been defined such as pH interval of 3–5, but no acid rebound provocation; fast onset of action; long - lasting efficacy; high neutralization potential and capacity.⁹ These are some of the factors necessary for the preparation of modern antacid formulations. This variability amongst antacids can be compared by analyzing preliminary antacid test (PAT)¹⁰, acid neutralizing capacity (ANC)¹⁰ and acid neutralizing potential (ANP) efficiencies of the antacids. For PAT, if the antacid - acid solution shows pH above 5, the antacid may provoke acid rebound and result in adverse effects such as bloating, meteorism and eructation.

a) Preliminary Antacid Test (PAT)

Minimum labeled dose (10g) was added to a beaker with 10 mL of distilled water and the solution was stirred while allowing the reaction to subside. The volume was then made up to 40 ml using Distilled water and the mixture was stirred at 300±30 rpm for about one minute.¹¹ 10 ml of 0.5N HCl was added to the test solution while stirring on magnetic stirrer at 300±30 rpm.¹¹ The stirring was continued for 10 min. After 10 min the pH was recorded using pH meter calibrated at 4.0.¹¹ The pH was noted down. The samples were further processed for acid neutralization potential and acid neutralization capacity if the pH recorded was 3 - 5.

Table 5

Formulation	pH after 10 mins	pH after 60 mins
F1	3.5	1
F2	5	4
F3	4.3	3.7
F4	4	3.8
F5	4.1	3.6
F6	4.3	3.5
F7	4.7	3.7

PAT is used to classify the formulations as potent antacids. Out of the 7 formulations, F1 showed pH as low as 1. This formulation will not be considered as potent antacid according to US pharmacopoeia definition of classifying and defining formulations as antacids. This formulation will also not be considered for calculating ANC and ANP. The pH of other samples was significant (3 - 5) to consider the formulations as antacids. Of all the tested samples, F2 (4), F3 (3.7), F4 (3.8), F5 (3.6), F6 (3.5), F7 (3.7) showed pH between 3 and 5. According to the literature, the antacid formulations should have pH between 3 and 5. All the formulations passing the criteria would be carried out for ANC and ANP. The formulation showing the best and potent results will be selected as the antacid of choice.

3. Result and Discussion

Preliminary Antacid Test (PAT)

The pH of the all the seven formulations was recorded after an interval of 10 minutes and after 60 minutes. The pH was found to be; F1 after 10 min were 3.5 and after 60 min were 1. The pH of F2 and F4 after 10 min was 5 and 4.3 and after 60 min were 4 and 3.7 respectively. The pH after 10 minutes was recorded to be 4 and after 60 min to be 3.8 for F4. The pH was 4.1 and 3.6 after 10 min and after 60 min respectively for F5. The pH of F6 was 4.3 after 10 min and 3.5 after 60 min. The pH after 10 minutes were 4.7 and pH after 60 minutes were 3.7 for F7. In the preliminary antacid test (PAT), the pH of all the formulations was found in the range of 3 - 5 except for F1. PAT was used to classify the formulation as potent antacid. All the formulations will be further tested for ANC and ANP except for F1.

4. Conclusion

The symptomatic relief for acid reflux or commonly called as acidity, is existent in many different dosage forms. The most common relief is attained by using antacid tablets or

effervescent granules. This study establishes the significance of use of effervescent granules for efficient treatment of acidity. The main aim and objective of the research is to incorporate herbal constituents such as cumin, sprague, and peppermint into the effervescent mixture for a more enhanced and prolonged effect of the antacid property into the gut. No such formulation is available in the market, as of now, considering herbal effervescent granules as a product. The herbal constituents used in the study are *Cuminum cyminum*, *Trachyspermum ammi*, and *Mentha piperata L.* which were shown to have additional properties which are good for the gut lining and help in treating acidity. These herbs are also used in daily lifestyle as home remedies against acidity, making them more trustworthy for usage. The seeds of Cumin (*Cuminum cyminum*) exhibit carminative, eupeptic, antispasmodic, astringent properties and used in the treatment of mild digestive disorders, diarrhoea, dyspepsia, flatulence, morning sickness, colic, dyspeptic headache and bloating, and are said to promote the assimilation of other herbs and to improve liver function. The Sprague (*Trachyspermum ammi*) leaves and seeds are proven to be beneficial in stomach troubles and possess stimulant and carminative properties. Sprague was reported as an anthelmintic medicine and also antidote for various natural toxic agents. *Mentha piperata L.* or more commonly known as peppermint also has some useful properties when it comes to curing acidity. Peppermint has been known as disorders improving including: analgesic, ulcer, anti - spasmodic, anti - bloat, irritable bowel syndrome or gastrointestinal motility, and immune system stimulant and etc. These herbal effervescent granules will prove to be of great use, as there is lot more trust of the South Asian population on the Ayurvedic systems and growing acceptance towards it. These formulations have successfully proven to treat acidity so far by satisfying the required criteria. This new study will open doors to more research and introduction of herbal based antacids in the market.