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Evaluation of Antacid Potential of Ayurvedic Poly-Herbal Formulation for Functional Dyspepsia

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Authors' contributions

This work was carried out in collaboration between all authors. Author AK designed the study, wrote the protocol and wrote the first draft of the manuscript. Author DP performed experiments (preparation and evaluation of avipattikar suspensions) author SW evaluated acid neutralization capacity of avipattikar suspensions. Author AK has conceived the idea, managed the literature searches and finalized the final draft of the article. All authors read and approved the final manuscript.

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ABSTRACT

Aim: Ayurveda describes herbal or polyherbal or herbo-mineral medicines such as Avipattikar churna for treatment of Amlapitta, ajirna for centuries. Ayurvedic medicines are associated with limitations namely, palatability, stability and accuracy of dose. Ayurvedic medicines lack in adequate safety and efficacy evidence data. The aim of the study was to develop a stable and palatable Avipattikar suspension using recent formulation and analytical techniques. The study was also aimed at determination of acid neutralizing capacity of Avipattikar suspension and predicting its efficacy for treatment of Functional Dyspepsia and Gastroesophageal Reflux Disorder. **Methods:** Flocculated Avipattikar suspension was prepared using sodium carboxymethylcellulose (CMC) as the suspending agent, sodium citrate as the flocculating agent, mannitol as a taste masking agent. Sodium carboxymethylcellulose, sodium citrate, Tween 80®, glycerin and mannitol were not used in Deflocculated Avipattikar suspension. The sedimentation volume, degree of flocculation, redispersibility and pH of the suspension was evaluated. The acid neutralization capacity of Avipattikar suspension was determined by Unite States Pharmacopoeia method.

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Results: The present study successfully demonstrated formulation of stable Avipattikar suspension from Avipattikar churna. The suspendability of sediment was retained for 15 days in presence of CMC. The results indicated that the acid neutralizing capacity of Avipattikar suspension (2.80 mMol of H^+/ gm) was similar to that of the marketed antacid suspension (2.756 mMol of H^+/ gm). The unpleasant taste of herbal drugs was masked satisfactorily.
Conclusion: Avipattikar suspension may be a cheaper, safer and effective alternative for current antacids for the treatment of functional dyspepsia.

Keywords: Acid related diseases; functional dyspepsia; ayurvedic; acid neutralizing capacity; Avipattikar suspension.

1. INTRODUCTION

Dyspepsia is one of the most commonly encountered conditions by the gastroenterologists, general physicians as well as the physicians of Traditional systems of medicines [1]. An organic cause for dyspepsia is observed in very few patients. The majority of the patients are diagnosed as Functional Dyspepsia (FD) [2]. Gastroesophageal Reflux Disease (GERD) and Functional Dyspepsia often coexist or overlap [3]. FD is a condition in which symptoms occur in upper abdomen, in the absence of organic disease that explains them. Gastroesophageal Reflux Disease (GERD) is a condition which develops when the reflux of stomach contents causes troublesome symptoms or conditions. FD affects millions of people worldwide [4]. The global prevalence of FD is about 20-30% [5], whereas the prevalence of FD, in Indian population, is 30.4% [6].

Proton Pump Inhibitors (PPIs), Histamine 2 receptor (H2) blockers, prokinetics and antacids are prescribed to relieve the symptoms of GERD and FD [7]. Although PPIs and H_2- blockers have been widely used, evidence from systematic review of randomized clinical trials suggests that PPIs have marginally better efficacy as compared to placebo and may be slightly more effective than prokinetics [8]. Previous studies have reported that metoclopramide [7] is not effective in FD. Long term use of PPIs and antacids has been associated with side effects [9,10]. Herbal antacids may be a cheaper, safer and effective alternative for current antacids since they reduce gastric acidity. Hence herbal actives may be preferred [11].

Ayurveda describes diseases amlapitta, ajirna [12,13] having symptoms similar to GERD and FD. Ayurveda prescribes many single herb or polyherbal or herbo-mineral medicines that have been used for centuries for treatment of acid related disorders. These medicines are available as wati (tablets), churna (powders), liquids [13,14]. Ayurvedic medicines suffer a setback due to issues related to the palatability, stability and accuracy of dose. In addition, Ayurvedic medicines lack in adequate safety and efficacy evidence data.

Avipattikar churna is a traditional polyherbal Ayurvedic medicine and is used for treatment of peptic ulcers [14]. It contains shunthi *(Zingiber officinale)*, maricha *(Piper nigrum)*, pippali *(Piper longum)*, haritaki *(Terminalia chebula)*, vibhitaka *(Terminalia bellerica)*, amalaki *(Emblica officinalis)*, musta *(Cyperus rotundus)*, vidanga *(Embelia ribes)*, ellayachi *(Elettaria cardamomum)*, patra *(Cinnamomum tamala)*, lavanga *(Syzygium aromaticum)*, trivrit *(Operculina terpethum),* salt *(Bid lavana)* and sharkara (sugar candy). All the herbal ingredients are used in 1 part except lavanga is used in 11 parts, trivrit is used in 44 parts and sugar candy is used in 66 parts respectively. Dose of Avipattikar churna is 3- 6 gm with water, before or after meals [15].

The purpose of this research was to formulate oral Avipattikar suspension for overcoming the limitations of Avipattikar churna and to improve the palatability. Another objective of the study was to determine the acid neutralizing capacity of Avipattikar suspension and compare it with an existing OTC antacid product to evaluate antacid potential of Avipattikar suspension.

2. MATERIALS AND METHODS

Zingiber officinalis rhizome powder, *Piper nigrum* fruit powder, *Piper longum* fruit powder, *Terminelia chebula* fruit powder, *Terminelia bellirica* fruit powder, *Emblica officinalis* fruit powder, *Cyperus rotundus* rhizomes powder, *Elettaria cardamomum* seed powder, *Cinnmomum tamala* leaf powder, *Syzygium aromaticum* floral bud powder, *Embelia ribes* fruit powder, *Operculina terpethum* root powder and

bid lavana were procured from Shree Sai Enterprises, Pune-38. Sodium carboxymethylcellulose (sodium CMC) was purchased from Bhortek Chemicals, Pune-21. Tween 80®, glycerin, methyl paraben, propyl paraben, disodium EDTA, sodium citrate, mannitol IP were supplied by Analab Fine Chemicals, Mumbai-53. Tricaine Mps Oral Gel®, manufactured by RPG Life Sciences Ltd., was purchased from local market. All other chemicals were of analytical grade.

2.1 Characterization of Herbal Drugs

The herbal drugs were subjected to quality control tests such as appearance, organoleptic characters, determination of foreign organic matter, ethanol soluble extractive, water soluble extractive, ash content, acid insoluble ash, loss on drying, heavy metals, microbial contamination [16], pesticide residue [17].

2.2 Formulation of Flocculated and Deflocculated Avipattikar Suspensions

Flocculated Avipattikar Suspension, containing 220 mg/ml or 6.655 gm/ 30 ml of herbal powders, was prepared. (Table 1) Initially, the herbal powders were weighed and mixed in geometrical proportion in the pestle-mortar. Tween 80® and glycerin were added to the powder mixture followed by sodium CMC, sodium citrate and mannitol were incorporated in the wet slurry. Methyl paraben, propyl paraben and disodium EDTA were added to the wet mixture and triturated with water to form a smooth dispersion. Water was added gradually while triturating.

Deflocculated Avipattikar suspension, consisting of herbal powders and *bid lavana*, was prepared by similar method. However, sodium CMC, sodium citrate, Tween 80®, glycerin, and mannitol were not incorporated. (Table 1) To reduce the batch to batch variation, each type of Avipattikar suspension (flocculated and deflocculated) was prepared thrice and the suspensions (number 6) were stored separately in amber glass bottles at room temperature till further analysis.

2.3 Evaluation of Avipattikar Suspensions

The organoleptic properties (e.g. colour, odour, and appearance) of Flocculated and Deflocculated Avipattikar Suspensions were observed by sensory organs. The pH of the suspensions was measured using Digital pH meter (EQ-610, Equip Tronics, Mumbai) [18]. Viscosity of the suspensions was determined using Brookfield viscometer at 20 rpm with spindle No. 2 [18]. The sedimentation volume, degree of flocculation and redispersibility of Avipattikar suspensions were determined as follows.

(a) Sedimentation volume: Avipattikar suspension was homogenized (by manual shaking) and transferred into a graduated Nessler's cylinder. The height of the sediment was observed daily for 15 days. Sedimentation volume is defined as the ratio of the final settled volume to the original volume and was calculated using following equation [18].

$$\text{Sedimentation volume } F = Vu / V_0$$

Where, Vu = Final volume of the sediment, Vo = Initial volume of the sediment

(b) Degree of flocculation: It is the ratio of the sedimentation volume of the flocculated suspension (F) to the sedimentation volume of the deflocculated suspension (F∞). Avipattikar suspension, containing sodium CMC and sodium citrate, was a flocculated suspension whereas Avipattikar suspension, without sodium CMC and sodium citrate, was a deflocculated suspension. The equation was used for degree of flocculation [18].

$$\text{Degree of flocculation } \beta = F / F\infty$$

Where F and F∞ are the sedimentation volume of flocculated and deflocculated suspensions, respectively

(c) Redispersibility: The redispersibility was determined by filling Avipattikar suspension in a glass vial and rotating the vial periodically around 360 degrees until thorough dispersion was achieved. The number of rotations (N) needed for complete redispersion was recorded. Redispersion was evaluated by visual observation [19].

2.4 Determination of Acid Neutralizing Capacity of Avipattikar Suspensions and Marketed Antacid Suspension

Avipattikar suspensions, flocculated as well as deflocculated, and marketed antacid suspension

(5.0 g) was dispersed in 100ml of water, heated to 37º C, and mixed with 100.0ml of 0.1M hydrochloric acid previously heated to 37º C. The solution was stirred continuously, maintaining the temperature at 37º C. The pH of the solution was recorded at 37º C, after 10, 15 and 20 minutes, and the pH was not less than 1.8, 2.3 and 3.0 respectively and at no time the pH was more than 4.5. This was followed by addition of 10.0ml of 0.5 M hydrochloric acid previously heated to 37º C, continuous stirring for 1 hour while maintaining the temperature at 37º C. The solution was titrated with 0.1M sodium hydroxide till the pH of the solution was 3.5 and the volume of sodium hydroxide was recorded [20,21].

2.5 Sensory Evaluation of Taste Masked Avipattikar Suspension

A sensory evaluation test was performed for confirmation of taste masking of flocculated and deflocculated Avipattikar suspensions. Bitterness of Avipattikar suspensions was measured by the taste panel of six healthy human volunteers from whom a written consent was obtained. The volunteers were instructed to keep 5 ml of flocculated Avipattikar suspension in the center of the tongue and not to swallow it. It was asked to retain in the mouth for 30 second, and then the mouth was thoroughly rinsed with distilled water. The response of the volunteers were recorded on the bitterness scale (0 =good, 1=tasteless, 2=slightly bitter, 3=bitter, 4=very bitter) [22]. The volunteers followed similar procedure while tasting De flocculated Avipattikar suspension.

3. RESULTS AND DISCUSSION

3.1 Characterization of Herbal Drugs

The results indicated that *Zingiber officinalis, Piper nigrum, Piper longum, Emblica officinalis, Terminelia chebula, Terminelia bellirica, Embelia ribes, Elettaria cardamomum, Syzygium aromaticum* complied with pharmacopoeial specifications [16]. (results not revealed) *Cinnmomum tamala* was characterized by Koppala et al [23], *Operculina terpethum* was characterized by Ashok Kumar et al [24], and *Cyperus rotundus* was studied by N. Anupama et al. [25]. Our results were corroborating with their results. *Bid lavana* complied with the physico-chemical properties described by Kawasthe et al. [26].

Table 1. Formulation of Flocculated and Deflocculated Avipattikar Suspensions

Sr. no	Ingredients	Flocculated Avipattikar Suspension	Deflocculated Avipattikar Suspension
1	*Zingiber officinalis*	100mg	100mg
2	*Piper nigrum*	100mg	100mg
3	*Piper longum*	100mg	100mg
4	*Emblica officinalis*	100mg	100mg
5	*Terminelia chebula*	100mg	100mg
6	*Terminelia bellirica*	100mg	100mg
7	*Cyperus rotundus*	100mg	100mg
8	*Emblia ribes*	100mg	100mg
9	*Elettaria cardamomum*	100mg	100mg
10	*Syzigium aromaticum*	1100mg	1100mg
11	*Cinnmomum tamala*	100mg	100mg
12	*Bid lavana*	100mg	100mg
13	*Operculina terpethum*	4400mg	4400mg
14	Sodium CMC (%)	0.5	--
15	Tween 80® (%)	0.5	--
16	Glycerine (%)	10	--
17	Sodium citrate (%)	1.5	--
18	Methyl paraben (%)	0.1	0.1
19	Propyl paraben (%)	0.01	0.01
20	Disodium EDTA (%)	0.1	0.1
21	Mannitol (%)	5	--
22	Distilled water to make up to (ml)	30	30

3.2 Formulation of Flocculated and Deflocculated Avipattikar Suspensions

Classical texts of Ayurveda describe Avipattikar churna/ powder and it is available in the market [15]. However, churna is associated with disadvantages such as inconvenience during transportation, difficulty in oral administration, non-uniformity of doses during repeated administration, unpalatable taste of plant drugs. The disadvantages of powders can be overcome by compressing the plant powders into a tablet. Therapeutic dose of Avipattikar churna, for treatment of peptic ulcer, is 3- 8 g with water, before or after meals. If herbal powders of such a large dose are compressed, it would result into a large tablet. It leads to difficulty in swallowing in but geriatric and paediatric patients. An aqueous suspension is a suitable alternative for administering drugs which are water insoluble and whose dose is relatively high. Suspension, consisting of high solids, can be administered easily if they are pharmaceutically elegant [18].

During the preparation of physically stable suspensions, a number of formulation components are used to keep the solid particles in a state of suspension (e.g. wetting agent, suspending agent, flocculating agent, viscosity imparting agent) while other components are added to vehicle itself and serve other functions (e.g. pH control agent and buffers, osmotic agent, preservative, colouring agent, flavour, and sweetening agent) [18].

The suspension is prepared by any one of the three methods namely, using a structured vehicle, using controlled flocculation, combination of both of structured vehicle and controlled flocculation [18].

Structured vehicles are aqueous dispersions of natural and synthetic gums and they increase the viscosity of the suspension. The aqueous dispersions of gums entrap the insoluble solid particles and reduce the sedimentation of the particles. Although, the structured vehicles improve dispersion of particles in water, they are unable to avoid the particle settling. As a result, a hard cake is formed upon storage of suspension for fairly long duration. Controlled flocculation of solid particles is obtained by inclusion of flocculating agents. The flocculating agents are of three types (1) Electrolytes (2) Surfactants (3) Polymers. Electrolytes surround the solid particles, decrease the repulsive forces between the particles and make the particles to come together to from loosely arranged flocs. The floccules remain suspended/ dispersed in aqueous phase for longer time. Obviously the suspension, which uses combination of structured vehicle and flocculating agent, produces highly stable suspension. Deflocculated suspension contains neither wetting and suspending agents nor the flocculating agent.

The aim of the present study was to develop taste masked, stable oral suspension, consisting of insoluble herbal powders. We have incorporated both hydrophilic polymer (sodium CMC) and flocculating agent (sodium citrate) in flocculated Avipattikar Suspension. Also Tween 80® (wetting agent), sodium citrate (flocculating agent), glycerin (viscosity imparting agent), mannitol (taste masking agent) were added to the flocculated suspension. These additives were not used in deflocculated suspension. Liquid orals may favor microbial growth [27-29]. Methyl and propyl paraben, along with disodium EDTA (stabilizing agent) were incorporated as preservatives in both types of suspensions.

3.3 Evaluation of Flocculated and Deflocculated Avipattikar Suspensions

Liquid suspension shows stability issues associated with maintaining the drugs in suspended state. Poorly formulated pharmaceutical suspensions enable the medication to settle as a residue and may not redisperse effectively, thus influencing the drug's therapeutic concentration in suspension. This can lead in the patient being underdosed or overdosed. It is therefore necessary to study the settling behaviour of the suspensions. "Stable" means that the dispersed phase (herbal powders) and the aqueous phase are not separated after preparation for a minimum period of time, or if separation occurs, the suspending agent can easily disperse the herbal powders with a small amount of agitation. They should be stable for at least 3 hours after preparing, preferably stable for at least 1 day after preparing, and preferably stable for at least 15 days after preparing.

The results indicated that flocculated Avipattikar suspension is stable. The suspensions showed brownish color, cloudy appearance and agreeable but characteristic odor of herbal powders. (Table 2) The powders were

homogeneously dispersed in flocculated suspension for 15 days whereas the powders formed a compact cake in deflocculated suspension after 2 days. The pH of flocculated and deflocculated suspension was 4.4 and 4.3 respectively. It was concluded that the excipients, incorporated for developing a flocculated suspension, have an insignificant effect on pH of the suspension. (Table 2)

Deflocculated suspension revealed lesser sedimentation volume and higher redispersibility and was attributed to the absence of the suspending agent, flocculating agent, viscosity imparting agent. (Table 2) Flocculated suspension, consisting of sodium CMC, sodium citrate, glycerin, depicted highest sedimentation volume after 15 days. Degree of flocculation of flocculated suspension was more than 1 indicating its stability. (Table 2) Redispersibility is commonly used for evaluation of the acceptability of suspension. Regarding the ease of redispersion of cake, flocculated suspension was easily redispersible than deflocculated suspension.

Sodium CMC, the suspending agent, and glycerin increase the viscosity of flocculated Avipattikar suspension and reduce the rate of particle sedimentation. Avipattikar churna contains an electrolyte *bid lavana* Kolkady et al. [30] have reported that *bid lavana* is not ammonium chloride, but it is sodium chloride.

According to Indian traditional system of medicine, *Operculina turpethum* is used to treat various ailments including pain, peptic ulcer and inflammation. The anti-ulcer, anti-secretory activity of the plant is very well studied and reported by Vidya Ignatius et al. [31]. Borhade et al. [32] have reported that starch grains are present in cortical cells of *Operculina turpethum* root powder. It may act as a suspending agent due to presence of starch grains.

Our study indicated that the degree of flocculation of flocculated Avipattikar suspension was very high (1.149). We propose that *bid lavana*, which is a salt, acts as the flocculating agent in Avipattikar suspension. Further, starch from *Operculina turpethum* root powder is gelatinized in presence of *bid lavana* and water. Gelatinized starch increases the viscosity of flocculated Avipattikar suspension (73.4 cps) and helps in suspending the insoluble powder. The electrolytes, sodium citrate and *bid lavana*, as well as *Operculina turpethum* improve the stability of Avipattikar suspension.

3.4 Determination of Acid Neutralizing Capacity of Avipattikar Suspension and Marketed Antacid Suspension

The acid neutralization equivalent of flocculated and deflocculated Avipattikar suspension (2.8 and 2.688 mMol of H^+/ gm respectively), was similar to the acid neutralization equivalent of marketed suspension (2.756 mMol of H^+/ gm). However, the pH of flocculated Avipattikar suspension, after addition of 100.0ml of 0.1 M hydrochloric acid, was higher (3.1) than the pH of marketed suspension (2.4). (Table 3) It revealed the higher antacid potential of flocculated Avipattikar suspension as compared to the marketed suspension. The pH of deflocculated Avipattikar suspension, after addition of 100.0ml of 0.1 M hydrochloric acid, was higher (3.68) than the pH of marketed suspension (2.4) and flocculated Avipattikar suspension (3.1). (Table 3) However, deflocculated Avipattikar suspension was unable to comply with the stability of suspensions.

The efficacy of antacids is correlated with their ability to neutralize stomach acid and to increase the pH of gastric contents. Hence the acid neutralization capacity of an antacid should be high. Antacid should neutralize gastric acid rapidly. Antacids do not neutralize gastric acid completely. However, if an antacid increases the gastric pH from 1.3 to 2.3 or to 3.3, it neutralizes 90% and 99% of gastric acid respectively. Most physicians believe in maintenance of gastric pH at about 3-3.5 for optimal healing of peptic ulcers [33,34]. It was concluded that flocculated Avipattikar suspension is effective in treatment of acid related disorders.

The antacid potential of Avipattikar suspension may be attributed to the presence of large number of phytoconstituents with anti-secretory, anti-ulcerogenic and gastroprotective properties. It is reported that haritaki, maricha and pippali exert cytoprotective effects on the gastric mucosa. Shunthi decreases the gastric secretion, increases the mucosal resistance and potentiates the defensive factors of the gastric mucosa. Lavanga helps in maintaining the basal gastric mucosal blood flow and it increases the mucus secretion [24,26,35]. *Operculina terpethum* is the major component (4.4 gm) of Avipattikar suspension.

Table 2. Evaluation of Avipattikar Suspensions

Sr. no.	Evaluation parameter	Flocculated Avipattikar suspension	Deflocculated Avipattikar suspension
1.	Colour	Brownish	Brownish
	Odour	Characteristic	Characteristic
	Appearance	Cloudy	Cloudy
2.	pH	4.4	4.3
3.	Sedimentation volume*	0.70±0.0057	0.65±0.021
4.	Degree of flocculation*	1.149±0.0284	--
5.	Redispersibility (N)*	17±1.8841	37±1.8856
6.	Viscosity (cPs)*	73.4±0.2222	23.61±0.8889

**Each observation indicates average of 3 readings ± standard deviation*

Table 3. Acid Neutralizing Capacity of Avipattikar Suspensions and Marketed Antacid Suspension

Sr. no	pH after	Flocculated Avipattikar Suspension	Deflocculated Avipattikar Suspension	Marketed Antacid Suspension	Specifications
1	10 min	2.1	3.68	2.1	pH should not be less than 1.8 and not more than 4.5
2	15 min	2.6	3.68	2.2	pH should not be less than 2.3 and not more than 4.5
3	20 min	3.1	3.8	2.4	pH should not be less than 3.0 and not more than 4.5
4	Volume of 0.1M sodium hydroxide	10 ml	5.6 ml	12.2ml	**N**ot more than 50.0ml of 0.1M sodium hydroxide

Table 4. Sensory Evaluation of Taste Masked Avipattikar Suspension

Sr. No.		Number of Volunteers Rating the Preparation as *				
		0	**1**	**2**	**3**	**4**
1	Flocculated Avipattikar Suspension	4	2	------	-----	-----
2	Deflocculated Avipattikar Suspension	--	--	3	3	----

**0= Good, 1= Tasteless, 2= Slightly Bitter, 3= Bitter, 4= very bitter*

3.5 Sensory Evaluation of Taste Masked Avipattikar Suspension

When flocculated Avipattikar Suspension was subjected to sensory evaluation by human volunteers, the volunteers did not feel any bitter taste after keeping the suspension in mouth for 30 seconds, which confirmed that bitter taste of herbal drugs was masked successfully. (Table 4)

4. CONCLUSION

The present study successfully demonstrated formulation of stable Avipattikar suspension from Avipattikar churna. It indicated masking of the bitter taste of the herbal drugs. The acid neutralization capacity of Avipattikar suspension was similar to that of the marketed antacid suspension. However, the improvement in the pH of gastric contents was higher in presence of

Avipattikar suspension than the marketed antacid suspension. It revealed the higher antacid potential of Avipattikar suspension. Avipattikar suspension may be a cheaper, safer and effective alternative for current antacids for the treatment of functional dyspepsia.

Further study including measurement of the intragastric pH, in presence and absence of Avipattikar suspension is needed. The study will be helpful in understanding role of Avipattikar suspension in increasing the gastric pH.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

CONSENT

As per international standard or university standard, respondents' written consent has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Harmon RC, Peura DA. Evaluation and management of dyspepsia. Ther Adv Gastroenterol. 2010;3(2):8798.
   DOI: 10.1177/ 1756283X09356590.
2. Kumar A, Patel J, Sawant P. Epidemiology of functional dyspepsia. Supplement To Japi. 2012; 60:9-12.
3. Takeuchi T, Takahashi Y, Kawaguchi S, Ota K, Harada S, Kojima Y. Therapy of gastroesophageal reflux disease and functional dyspepsia overlaps with symptoms after usual-dose proton pump inhibitor: Acotiamide plus usual-dose proton pump inhibitor *versus* double-dose proton pump inhibitor. J Gastroenterol Hepatol. 2018;33(3):623-630.
   DOI: 10.1111/jgh.13970.
4. Hiroto M, Ghoshal UC, Gonlachanvit S, Kok-Ann Gwee, Ting-Leong Ang, Full-Young Chang, Kwong Ming Fock, Michio Hongo, Xiaohua Hou, Udom Kachintorn, Meiyun Ke, Kwok-Hung Lai, Kwang Jae Lee, Ching-Liang Lu, Sanjiv Mahadeva, Soichiro Miura, Hyojin Park, Poong-Lyul Rhee, Kentaro Sugano, Ratha-korn Vilaichone, Benjamin CY Wong, Young-Tae Bak. Asian consensus report on functional dyspepsia. J Neurogastroenterology and Motility. 2012;18(2):150-168.
   http://dx.doi.org/10.5056/jnm.2012.18.2.150.
5. Kahrilas PJ. Gastroesophageal reflux disease. New England Journal of Medicine. 2008; 359(16):1700–1707.
   DOI:10.1056/NEJMcp0804684.
6. Madisch A, Andresen V, Enck P, Labenz J, Frieling T, Schemann M. The diagnosis and treatment of functional dyspepsia. Dtsch Arztebl Int. 2018;115:222–32.
   DOI: 10.3238/arztebl.2018.0222.
7. Yamawaki H, Futagami S, Wakabayashi M, Sakasegawa N, Agawa S, Higuchi K, Kodaka Y, Iwakiri K. Management of functional dyspepsia: state of the art and emerging therapies. Ther Adv Chronic Dis. 2018;9(1):23–32.
   DOI: 10.1177/2040622317725479.
8. Pinto-Sanchez MI, Yuan Y, Hassan A, Bercik P, Moayyedi P. Proton pump inhibitors for functional dyspepsia (review). Cochrane Database of Systematic Reviews. 2017;(11).
   Art. No.: CD011194.
   doi: 10.1002/14651858.CD011194.pub3
9. Brunton LL, Hilal-Dandan R, Knollmann BC. Goodman and Gilman's: The Pharmacological Basics of Therapeutics. Ninth ed. New York: McGraw-Hill Health Professions Division; 1996; 910,911,1196.
10. Craig CR, Stitzel RE. Modern Pharmacology with Clinical Applications. Sixth ed. Baltimore: Lippincott Williams & Wilkins. 2003;478-479.
11. Yuan H, Qianqian Ma Li Ye, Guangchun P. The traditional medicine and modern medicine from natural products. Molecules. 2016;21:559-577.
    https:// doi: 10.3390/molecules21050559.
12. Acharya Sri Narendranath Shastri. Madhavnidanam-Madhavkar Praneet. 6th reprint. New Delhi: Motilal Banarsidas Publishers Private Limited. 2017;1:641. Verse 7,8,9: 226. Sanskrit
13. Ayurvedic Standard Treatment Guidelines. New Delhi: Ministry of Ayush, Government of India; 201;28.
14. Anonymous. The Ayurvedic Formulary of India: Part I. New Delhi: Ministry of Health

and Family Welfare, Govt of India. 2000;7/2.

15. Shri Ambika Datta Shastri and Shri Rajeshwar Datta Shastri. Ayurvedshashtracharya Bhaishajya Ratnavali with Vidyotini Hindi Commentary. Eighth edition. Varanasi: Chaukhambha Sanskrit Sanstha. 1987;24-7.
16. Indian Pharmacopoeia Volume III. Ministry of Health and Family Welfare Government of India. New Delhi: Indian Pharmacopoeia Commission Ghaziabad. 2014;2003, 2472,2484,2492,2518,2522,2530,2544,3174 ,3191,3218,3225,3237,32443255,3270,3280
17. Sharma A, Gaurav S, Balkrishna A. A rapid and simple scheme for the standardization of polyherbal drugs. Int J of Green Pharmacy. 2009;Apr-June:134-140.
18. Lachman L, Lieberman HA, Kanig JL, editors. The Theory and Practice of Industrial Pharmacy. Third ed. Philadelphia: Lea and Febiger. 2009;27-29.
19. Moghimipour E, Salimi A, Rezaee S, Balack M, Handali S. Influence of flocculating agents and structured vehicles on the physical stability and rheological behavior of nitrofurantoin suspension. Jundishapur Journal of Natural Pharmaceutical Products. 2014;9(2):e12716.
20. Kulkarni A, Pandit D, Walke S, Kolatkar A. Formulation and Evaluation of Oral Reconstitutable Avipattikar Suspension.
21. United States Pharmacopoeia National Formulary USP 30-NF 25. Rockville, MD: United States Pharmacopoeial Convention, Inc. 2007;301.
22. Gao Y, Cui FD, Guan Y, Yang L, Wang YS, Zhang LN. Preparation of roxithromycin polymeric microspheres by the emulsion solvent diffusion method for taste masking. International Journal of Pharmaceutics. 2006;318(1-2):62-9.
23. Koppala NSK, Maheshwari R, Billadi S, Basavaiah R, Raghuvrrra M. Chemical examination of leaves of *Cinnamomum malabatrum* blume sold as tamalapatra. Pharmacognosy Journal. 2012; 4(31):11-15.
24. Ashok Kumar BS, Prabhakaran V, Lakshman K, Nandeesh R, SaleemullaKhan, ManiTripathi MN, NarayanaSwamy VB, Subramanyam P. Histological and physic-chemical evaluation of *Operculina turpethum* Linn root. Ethnobotanical Leaflets. 2009;13:215-20.
25. Anupama N, Hema N, Ramakrishna A, Kumar KNS. Evaluation of physicochemical standards of *Cyperus rotundus* rhizome with phytochemical and HPTLC profiling of its extracts. International Research Journal of Pharmacy. 2013;4(6):133-137.
26. Kawashte AD, Gandhi PK. Pharmaceutico-analytical evaluation of the bid lavana- a herbomineral formulation. International Ayurvedic Medical Journal. 2017;1(4):423-433.
27. Udeze AO, Talatu M, Ezediokpu MN, Nwanze JC, Okonko I.O. The effect of *Klebsiella pneumoniae* on catfish. Researcher. 2012;4(4):51-59.
28. Ratanraj SM, Sunshine WL. Aqueous Pharmacetical Suspension and Process for Preparation Thereof. United States Patent 5658919 A; 1997.
29. Dastidar SG, Pal S, Basak S, Roy S, Roy DS, Palchoudhuri S. Experimental evaluation of practical viability of good manufacturing practices in preparation of oral liquid formulations in small scale pharmaceutical industries. European Journal of Pharmaceutical and Medicinal Research. 2016;3(4):403-407.
30. Kodlady N, Patgiri BJ, Galib R, Prajapati PK. Preparation of Vida Lavana and its Energy Dispersive X-ray Analysis. Annals of Ayurvedic Medicine. 2015;4(1):47-50.
31. Ignatius V, Narayanan M, Subramanian V, Periyasamy BM. Antiulcer Activity of Indigenous Plant Operculina turpethum Linn. Evidence-Based Complementary and Alternative Medicine. 2013:1-7.
32. Borhade RS, TA Deshmukh, Patil VR, Khandelwal KR. Pharmacognostic and Phytochemical Investigations of *Operculina turpethum* LINN. root. International Science of Pharmaceutical Journal and Research. 2014;5(6):2387-392.
33. Dubek JJ, McNally GP, Smith BP. Liquid antacid compositions. United States Patent 5914135; 1999.
34. Burget DW, Chiverton SG, Hunt RH. Is there an optimal degree of acid suppression for healing of duodenal ulcers? a model of the relationship between ulcer healing and acid suppression. Gastroenterology. 1990; 90:345-351.
35. Gyawali S, Khan GM, Lamichane S, Gautam J, Ghimire S, Adhikari R, Lamsal R. Evaluation of anti-secretory and anti-

ulcerogenic activities of avipattikar churna on the peptic ulcers in experimental rats. Journal of Clinical and Diagnostic Research. 2013;7(6):1136-1139.

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