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# Efficacy of *Pippalī* (Fruits of *Piper longum* Linn.) in *Grahaṇīroga*: A Prospective Open label Clinical Trial

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## ABSTRACT

**Introduction:** In the current epoch, the diseases allied to *Anna vaha* and *Purīṣavahasrota* (~gastrointestinal tract) are commonly found in clinical practice. Among of them *Grahaṇīroga* (~ Irritable bowel syndrome) is one of the most important disorder. This disease occurs due to the distorted function of *Agni* (~digestive power). Present study aimed to clinically evaluate the efficacy of *Pippalī* (*Piperlongum* Linn.) in *Grahaṇīroga*. **Methods:** Forty patients were selected from OPD and IPD of Institute of Post Graduate Ayurvedic Education and Research at Shyamadas Vaidya Shastra Pith, irrespective of their sex, religion and occupation based on inclusion and exclusion criteria. Patients satisfied the maximum symptoms for *Grahaṇīroga* mentioned in the classical *Āyurveda* texts were included in the study. Two gm powder of *Pippalī* fruit with plain water was administered in selected patients in two divided doses per day for a period of one month. All the patients were assessed for selected subjective and objective parameters to analyze the efficacy of the study drug. **Results:** After one month, all the subjective and objective parameters were evaluated. The efficacy of the stipulated drug on *Grahaṇīroga* was evaluated based on the statistical analysis. Study showed the test drug was significantly effective in various subjective parameters of *Grahaṇīroga* along with marked changes in laboratorial objective parameters like routine examination of stool. **Conclusion:** Powder of *Pippalī* is effective to improve the classical sign and symptoms of *Grahaṇīroga*. In analysis of objective parameters, no such marked changes were found, except in examination of stool.

## KEYWORDS

*Agni*, *Grahaṇīroga*, *Pippalī*, gastrointestinal system

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## INTRODUCTION

In the current era, the diseases allied to *Anna vaha* and *Purīṣavahasrota* (~gastrointestinal tract) are commonly found in clinical practice. Among of them *Grahaṇīroga* is one of the most important disorders. This disease occurs due to the distorted function of *Agni* (~digestive fire). Various scholars have opined that function of *Agni* (~digestive fire) can be evaluated through the analysis of gastric juice and different enzymes at Gastro intestinal level.<sup>[1]</sup> All of them are accountable for the physiological function of digestion, absorption and metabolism. Altered function of the enzymes secreted from Gastro intestinal tract is responsible for foundation of Gastro intestinal disorders. *Agni* (~digestive fire) is seated at the spectacle of *Grahaṇī* (the organ hold down the descending progress of the undigested food particles until it is exclusively digested.) which is situated above the umbilical region. The system *Grahaṇīs* supported and nurtured by the potency of *Agni*. Improper function of *Agni* put across the pathological condition like *Vidāha* (~The condition where a part of food particle become digested, whereas the other part remain in undigested condition which ultimately budes upwards and downwards in gastro-intestinal tract and produce burning sensation). The *Pakva* (~digested) and *Apakva* (~undigested) food particles moves downwards and ultimately manifests *Grahaṇīroga*.<sup>[2]</sup> In other words, *Agnicooks* any material located over it i.e. in *Āmāśaya* or stomach.<sup>[3]</sup> Till the food is digested, the organ *Grahaṇī* helps in its withholding in the upper part (stomach), and after digestion, the food is released to the intestinal tract through the sides of *Grahaṇī*. This liberate of processed foodstuff takes place from the left side of the *Grahaṇī* because both the *Grahaṇī* and *Guda* (~rectum including anus) are located in the left side of the stomach. Both *Āma* (~unprocessed) and *Pakva* (~digested) food products come out with the fecal material. When it is vitiated due to weakness of *Agni*, only *Apakva* (~undigested) food is perpetually voided and therefore formed several sign and symptoms of *Grahaṇīroga*.<sup>[4]</sup> To mitigate the pathogenesis of *Grahaṇīroga*, fruit powder of *Pippalī* was administered in this study. The drug *Pippalī*, botanically identified as *Piper longum* Linn. is a well known drug in *Āyurveda* mentioned by ancient classics and frequently practiced for the condition of *Agnimāndya* (~poor digestive power).<sup>[5]</sup> Hence the present study aimed to clinically evaluate the efficacy of *Pippalī* to improve the symptoms of *Grahaṇīroga*.

## MATERIALS AND METHODS

### Selection of the patients

Forty patients were selected from OPD and IPD of Institute of Post Graduate Ayurvedic Education and Research at Shyamadas Vaidya Shastra Pith strictly based on the fixed inclusion and exclusion criteria of the study.

### Study design

Prospective open label clinical trial was chosen.

### Inclusion criteria

1. Patient belonged to the age group of 16 years and above up to below 70 years.<sup>[6]</sup>
2. Patients primarily diagnosed as classical *Grahañiroga* with no other history of medications.
3. Patients presenting with cardinal symptoms *Muhurvaddham Muhurdravammalam* (frequently loose motion and constipation)<sup>[7]</sup> and macroscopically presenting undigested vegetable particles in stool.
4. Patients satisfied the maximum classical subjective criteria for *Grahañiroga*.

### Exclusion criteria

1. Patients those who were not willing to include themselves in the study.
2. Patients were suffering from any other major systemic disorders like Hepatic Failure, Renal Failure, Cardiac Disorder, Diabetes Mellitus, Malignancy and Thyroid Disorders etc.
3. Patients presenting the *Asādhyalakṣaṇa* (~symptoms indicating the poor prognosis).<sup>[8]</sup>
4. Patients were receiving any other supplementary therapy.

### Subjective parameters of *Grahañiroga*<sup>[9]</sup>

Patients those who were presenting cardinal symptoms of *Grahañiroga* associated with maximum numbers of the following subjective parameters were included in the study.

*Śuktapāka* (~sour eructation), *Kharāṅgatā* (~roughness), *Āsyaśoṣa* (~dryness of mouth), *Kaṅṭhaśoṣa* (~dryness of throat), *Kṣudhā* (~loss of appetite), *Tṛṣṇā* (~feeling of thirst), *Timira* (~loss of vision), *Karṇayoḥsvanaḥ* (~persisting sounds on ear), *Pārśvaūruvaṅkṣaṇagrīvārūka* (~pain in flank, chest, groin and neck region), *Visūcīkā* (~loose motion and vomiting with sever pricking pain), *Hṛdpidā* (~cardiac pain), *Gr̥ddhihsarvarasānām* (~desire for all tastes), *Mana Sadana* (~depression), *Jirṇe- jīryati ca ādhmānaṃ Bhuktēsāvāsthyamupaiti* (~after ingestion of food patient feel well but after digestion and during digestion urges of flatulence), *Cirādduḥkhamdravaṃśuṣkaṃtanuūmaśabdaphenavatvarca* (~sometimes hard and sometimes frothy stool with minimum quantity), *Kāsa* (~cough with sound like broken bronze pot.), *Ajīrṇa* (~indigestion), *Nīla-Pītābhampītābhaḥsāryatedravam* (~altered color of stool), *Pūtīamlaudgāra* (~foul smelling belching), *Bhinnaāmaśleṣmasaṃsṛṣṭa guru varcapravartanam* (~ill formed stool with mucus), *Akṛśasyāpīdaurbalya* (~despite lack of emaciation feels weak in sedentary work).

### Objective parameters of *Grahañiroga*

Several studies has concluded that function of *Agni* (~digestive fire) can be evaluated through the analysis of gastric juice and different enzymes at Gastro intestinal level because physiologically *Agni* is responsible factor for digestion, absorption and metabolism. Based on this, following laboratorial parameters were observed.

1. Examination of Stool for Routine Examination and Microscopic Examination (occult blood)
2. Biochemical tests:
  - a. L.F.T (Liver Function Test) with G.G.T (Gamma Glutamyl Transpeptidase)
  - b. Serum amylase
  - c. Serum Lipase

### Administration of drug

The patients were treated with two gms fruit powder of *Pippalī* with plain water in two divided doses per day, provided in between two meals, for a period of one month. All the patients were examined to evaluate the subjective and objective parameters after 7days, 15 days and 30 days of administration of test drug. The efficacy of the stipulated drug on *Grahañirogawas* evaluated based on statistical analysis.

### Assessment of subjective parameters for *Grahañiroga*

Subjective parameters mentioned in the classical Ayurveda texts were evaluated by the preliminary approach of arbitrary grading system. Appropriate literary meanings of each particular symptom were encompassed after methodical discussion with subjective experts to make the arbitrary grading (Table 2). An assessment scale was framed to assess the rate of improvement. At the end of management, the consequence in analysis of percentage of relief was classified under the subsequent headings (Table 1).

**Statistical analysis**

Effect test drug was evaluated by Statistical method 'Paired t-test'.

**Table 1. Assessment of percentage of relief and remarks**

Percentage of relief	Remark
100% improvement of subjective parameters.	Complete remission
>75%-100% improvement of subjective parameters.	Marked improvement
>50%-75% improvement of subjective parameters.	Moderate improvement
>25%-50% improvement of subjective parameters.	Mild improvement
Equal or <25% improvement of subjective parameters.	No improvement

**Table 2. Arbitrary grading of subjective parameters for *Grahanī roga***

SN	Sign and symptoms	Grade				
		0	1	2	3	4
1.	<i>Śuktapāka</i> ( <i>Amla pākam</i> = Sour eructation)	Sour eructation not occurs.	Sour eructation occurs occasionally in 24 hours.	Sour eructation occurs after an interval in 24 hours.	Sour eructation occurs continuously in 24 hours.	Sour eructation occurs continuously more than 24 hours.
2.	<i>Kharāṅgatā</i> ( <i>Karkaśa śarīratvaṃ, vātena tvaga gata sneha śoṣāt</i> = Roughness)	No Roughness.	Roughness due to atmosphere.	Roughness occurs occasionally.	Roughness during touch.	Visualized persisting roughness.
3.	<i>Kañṭha śoṣa, Āśya śoṣa</i> (Dryness of throat and mouth)	Dryness of throat and mouth not occurs.	Dryness of throat and mouth occurs some times in 24 hours.	Dryness of throat and mouth occurs 1 or 2 times in 24 hours.	Dryness of throat and mouth occurs after an interval of 24 hours.	Dryness of throat and mouth occurs all time in 24 hours.
4.	<i>Kṣudhā: (Kṣudhāyā abhāvaḥ</i> = Loss of Appetite)	Normal Appetite.	Loss of Appetite occurs 1 time in 24 hours.	Loss of Appetite occurs 2 times in 24 hours.	Loss of Appetite occurs 3 times in 24 hours.	Loss of Appetite occurs 4 times in 24 hours.
5.	<i>Trṣṇā (Pipāsa =Punah Punah Pibati</i> = Feeling of thirst).	Normal feeling of thirst.	Feeling of thirst 7-9 times/ 24 hours, either/ or intake of water 5-7 times / 24 hours with quantity 1.5-2 lit/ 24 hours.	Feeling of thirst 9-11 times/ 24 hours, either/ or intake of water 7-9 times / 24 hours with quantity 2-2.5 lit/ 24 hours.	Feeling of thirst 11-13 times/ 24 hours, either/ or intake of water 9-11 times / 24 hours with quantity 2.5-3 lit/ 24 hours.	Feeling of thirst >13 times/ 24 hours, either/ or intake of water >11 times/ 24 hours with quantity >3 lit/ 24 hours.
6.	<i>Timira (Manda drṣṭitā</i> = loss of vision.)	Vision without glass.	Vision with glass.	Vision with glass with blunt.	Blunt vision with systemic problem.	Complete loss of vision.
7.	<i>Karṇajohṣvanah</i> ( <i>Karṇau saśabdau</i> = Persisting sounds on ear)	Persisting sounds on ear not present.	Persisting sounds on ear present occasionally in 24 hours.	Persisting sounds on ear present intermittently in 24 hours.	Persisting sounds on ear present continuously 24 hours.	Persisting sounds on ear present continuously more than 24 hours.
8.	<i>Pārśvaūru vañkṣaṇa grīvā ruka (Pīḍā sā pārśvadibhiḥ samvadhyate</i> =Pain in flank chest groin and neck region).	Pain not occurs.	Occasionally pain in flank chest groin and neck region occurs in 24 hours.	In a particular time pain in flank chest groin and neck region occurs in 24 hours.	Intermittently pain in flank chest groin and neck region occurs in 24 hours.	Persisting pain in flank chest groin and neck region occurs more than 24 hours.
9.	<i>Hṛdpidā (Hṛdayaśulam gauravaṃ ca</i> = Cardiac pain)	Mild cardiac pain not occurs.	Mild cardiac pain occurs occasionally in 24 hours.	Mild cardiac pain occurs 2 to 3 times in 24 hours.	Mild cardiac pain persists 24 hours.	Mild cardiac pain persists more than 24 hours.

10.	<i>Grddhih sarvarasānām</i> (Grddhih kānkhā, sarvarasānām madhurādīnā =Desire for all tastes)	Desire for all tastes not occurs.	Desire for all tastes occurs occasionally in 24 hours.	Desire for all tastes occurs particular time in 24 hours.	Desire for all tastes occurs intermittently in 24 hours.	Desire for all tastes occurs all time in 24 hours.
11.	<i>Mana sadana</i> ( <i>Manoglānih</i> =Depression)	No depression.	Depression in unfavorable condition.	Depression in favorable condition.	Intermittent depression.	Continuous depression.
12.	<i>Kāsa</i> ( <i>Bhinna kāmasya pātravat hata svanaḥ</i> = Cough with sound like broken bronze pot.)	Cough with sound like broken bronze pot not occurs 24 hours.	Cough with sound like broken bronze pot persists occasionally in 24 hours.	Cough with sound like broken bronze pot persists intermittently in 24 hours.	Cough with sound like broken bronze pot persists 24 hours.	Cough with sound like broken bronze pot persists more than 24 hours.
13.	<i>Ajīrṇa</i> ( <i>Apakvam</i> = Indigestion)	Indigestion not occurs.	Persisting indigestion for 6 hours.	Persisting indigestion for 12 hours.	Persisting indigestion for 24 hours.	Persisting indigestion for more than 24 hours.
14.	<i>Nīlapītābhampītābhaḥ sāryate dravam</i> (Altered colour of stool).	Altered colour of stool not present	Altered colour of stool present occasionally in 24 hours	Altered colour of stool present 1 times in 24 hours.	Altered colour of stool present continuously in 24 hours.	Altered colour of stool present continuously more than 24 hours.
15.	<i>Pūti amlaudgāra:</i> ( <i>Sa dhūmodgārah</i> =Foul smelling belching).	Foul smelling belching not occurs.	Foul smelling belching occurs occasionally in 24 hours.	Foul smelling belching occurs intermittently in 24 hours.	Foul smelling belching occurs continuously 24 hours.	Foul smelling belching occurs continuously more than 24 hours.
16.	<i>Akrśasyāpi daurobalya</i> ( <i>Sthūlavato api karmani asamartham</i> =Despite lack of emaciation feels weak in sedentary work).	Symptoms absent.	Despite lack of emaciation feels weak in hard work.	Despite lack of emaciation feels weak in moderate work.	Despite lack of emaciation feels weak in mild work.	Despite lack of emaciation feels weak in sedentary work.

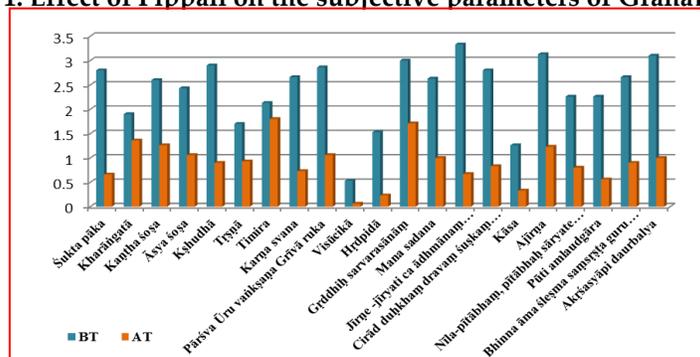
## RESULTS AND DISCUSSION

**Effect of drug on subjective parameters:** Effect of drug on subjective parameters were analyzed (Graph 1).

**Effect of drug on objective parameters:** Before and after administration of drug the biochemical parameters and examination of stool were performed. In analysis of objective parameters like serum bilirubin, SGPT, SGOT, alkaline phosphatase, prothrombin time, gamma glutamyl transpeptidase, serum amylase, serum lipase; data were found to be statistically insignificant ( $P>0.05$ ) and significant changes ( $P<0.001$  and  $P<0.01$ ) were observed in the parameters of serum proteins, serum albumin, serum globulin, albumin globulin ratio. Significant changes were also noticed in physical, microscopical and chemical parameters of stool. After completion of one month, undigested food materials were completely absent.

**Assessment of progress:** The assessment of progress was first noted at the end of 7th day, 15th day and 30th day i.e. after the course of treatment. An assessment scale was framed to assess the rate of improvement. Result obtained from the study is discussed (Table 1 and Graph 1).

**Graph 1. Effect of Pippalī on the subjective parameters of Grahaniroga**



To assess the state of *Grahañiroga* initial move towards arbitrary grading system were utilized. Where Grade 4 was considered as maximum severe condition and Grade 0 was considered as the minimum grave condition (table-2). After one month administration of drug marked and moderate improvement was observed. Study showed that the drug is significantly helpful in subjective parameters of *Grahañiroga* (Graph 1). Maximum subjective parameters were to be found statistically significant ( $P < 0.05$ ) except *Kharāṅgatā* (~roughness), *Trṣṇā* (~feeling of thirst), *Timira* (~loss of vision), *Visūcikā* (~loose motion and vomiting with sever pricking pain) where observed 'p' value was statistically insignificant ( $P > 0.05$ ). Significant changes of objective parameters were observed on examination of stool. Other parameters were found to be statistically insignificant. At the end of management, the result in view of percentage of relief was classified. Here in no such parameter 100% improvement was observed. Less than 100% to 75% i.e. marked improvement of subjective parameters were observed on the parameters of *Śuktapāka* (~sour eructation), *Visūcikā* (~loose motion and vomiting with sever pricking pain), *Hṛdpidā* (~cardiac pain), *Jirṇe- jīryati ca ādhmānambhuktesvāsthyamupaiti* (~after the ingestion of food patient feels well but after digestion and during digestion urge of flatulence). Moderate improvement ( $\geq 50\%$  -  $< 75\%$ ) was observed on the parameters of *Kaṅṭhaśoṣa* (~dryness of throat), *Āśyaśoṣa* (~dryness of mouth), *Kṣhudhā* (~loss of Appetite), *Karṇayoḥsvanaḥ* (~persisting sounds on ear), *Pārśvaūruvaṅkṣaṇagrīvārūka* (~pain in flank chest groin and neck region), *Grddhīhsarvarasānām* (~desire for all tastes), *Mana sadana* (~depression), *Cirādduhkhāmdravamaśuṣkamtanuāmasābdaphenavatvarca* (~sometimes hard and sometimes frothy stool with least quantity), *Kāsa* (~cough with sound like broken bronze pot), *Ajīrṇa* (~indigestion), *Nīla-pītābhampitābhaḥsāryatedravam* (~altered colour of stool), *Pūtiāmlaudgāra* (~foul smelling belching), *Bhinmāmasleśmasasrṣṭa guru varcapravartanam* (~ill formed stool with mucus), *Akrāsyaṅpīdaurbalya* (~despite lack of emaciation feels weak in sedentary work) likewise mild improvement ( $\geq 25\%$  -  $< 50\%$ ) was observed on the parameter of *Kharāṅgatā* (~roughness), *Trṣṇā* (~feeling of thirst).

The drug *Pippalī* is a renowned drug in *Āyurveda* due to its multidimensional exploit. The drug may acts through its *Kaṭu rasa* (~pungent taste), *Laghu* (~light), *Snigdha* (~unctuous), *Tikṣṇa* (~raggedness property), *Madhuravipāka* (~sweet metabolic transformation) and *Anuṣṇāvīrya* (~medium temperate active potency).<sup>[5]</sup> All the *Dravya* (~substances) are constituted by five *Mahābhūta* (~five basic elements). So, after scrutiny the *Pāñcabhautika* composition of *Pippalī*, it was observed that *Pippalī* have significant ability to alleviate the symptoms of *Grahañiroga* by its *Dīpana* (~stimulation of digestion), *Pācana* (~digestion and metabolism), *Rocana* (~craving), *Lekhana* (~scrap), *Vṛṇhana* (~nourishing) and *Śodhana* (~purification) *Karma* (~action). In *Āmāvasthā* (~unprocessed ingested food materials) the *Dīpana* (~stimulation of digestive process), *Pācana* (~absolute digestion), etc. *karma* and in *Pacyamānāvasthā* (~during the processing of ingested food materials) *Śodhana karma* (~action of purification) are meticulous (Fig. 1 and 2).

Figure 1. Mode of action of Pippalī

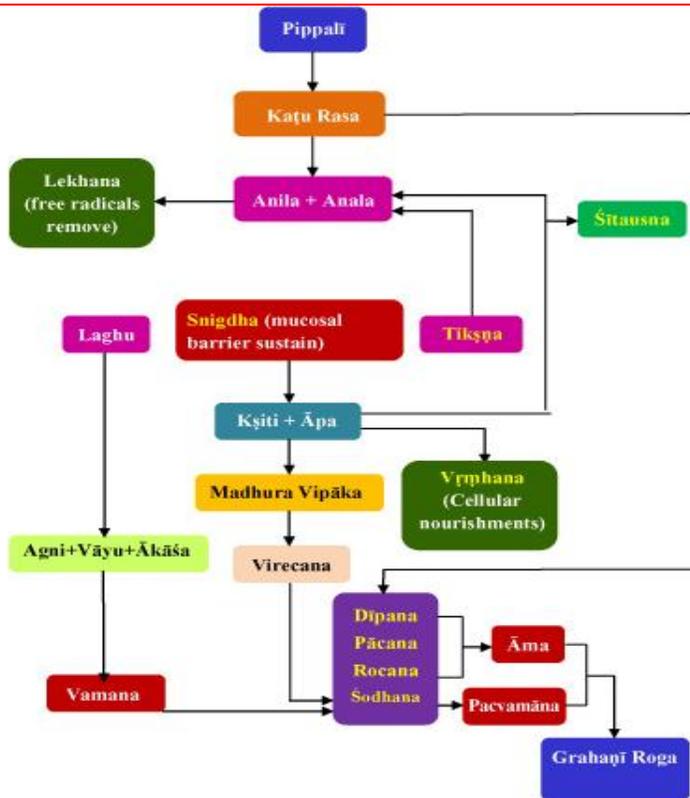
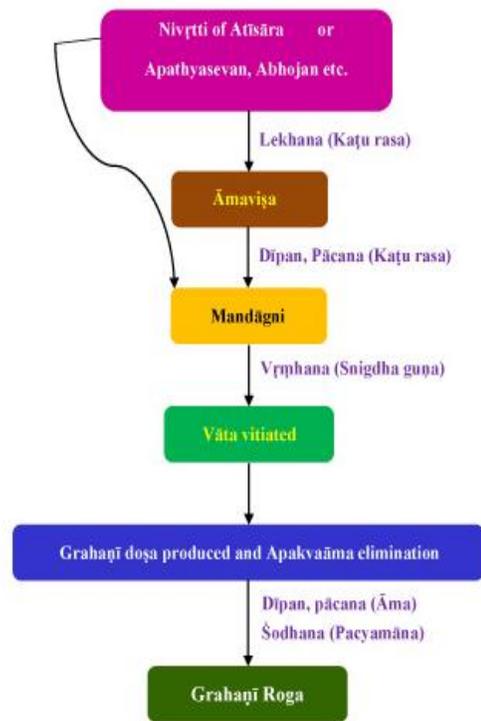


Figure 2. Samprāpti Vighaṭana of Grahañi roga



By virtue of these properties the drug was markedly effective in the symptoms like *Śuktapāka* (~sour eructation), *Visūcīkā* (~loose motion and vomiting with sever pricking pain), *Hṛdpidā* (~cardiac pain), *Jirṇe- jīryati ca ādhmānaṃ bhukte svāस्थ्यamupaiti* (~after the ingestion of food patient feel well but after digestion and during digestion urge of flatulence) etc.

## CONCLUSION

The present study ascertains that succeeding one-month administration of fruit powder of *Pippalī* (*Piper longum* Linn.) was significantly effective in improvement of subjective parameters of *Grahaṇīroga*. Ultimately, marked to moderate intensification was observed in the participants but no marked changes were found in most of the objective parameters of *Grahaṇīroga*, except in the parameters of Serum Proteins, Serum Albumin, Serum Globulin, Albumin Globulin ratio and physical, microscopical and chemical parameters of stool. Explanation behinds this may be the constraint of study like small sample size, short duration of study and few objective criteria were not found in every selected patient. Further study can undertake with special consideration of these limitations.

## CONFLICT OF INTEREST

Nil

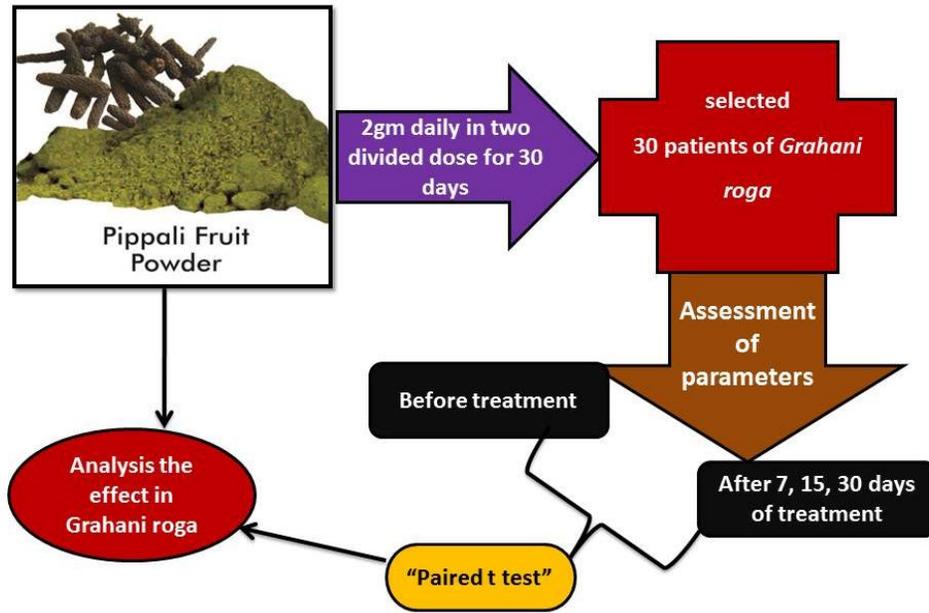
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**GRAPHICAL ABSTRACT**



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