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A COMPARATIVE STUDY OF DIGESTIVE STIMULANT ACTION OF MARICHA CHOORNA AND TRIKATU CHOORNA IN EXPERIMENTAL RATS

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ABSTRACT

In Ayurveda, there are so many formulations which play important role in gastrointestinal problems. Among them Trikatu choorna (combination of dried fruits of *Piper longum*, *Piper nigrum* and rhizomes of *Zingiber* officinale) is most commonly prescribed by ayurvedic practitioners for digestive impairment. Maricha is one of the three contents of Trikatu choorna. As Trikatu choorna and Maricha choorna both have Deepana (digestive stimulant) activity, this study was proposed to assess the digestive stimulant activity of Maricha choorna in comparison with Trikatu choorna. CMC (carboxy methyl cellulose) was used as a vehicle. The experiment was done on female Sprague Dawley Rats of body weight ranging 150-220 gms. Both the test drugs were administered to the animals of respected groups at 300mg/kg weight of rats b.d. for 7 days. On 8th day, blood samples and small intestinal mucosal scrapings of rats were taken for enzyme estimation with the help of standard enzyme estimation kits. The digestive enzymes namely alkaline phosphatase, lipase, amylase and protein content were estimated. The results show that both the choornas have definitive stimulatory action on digestive enzymes and Maricha choorna is having more lipolytic activity than Trikatu. It is more useful in fat digestion than Trikatu.

KEYWORDS: Choorna, Digestive stimulant, Experimental rats, Maricha, Trikatu.

INTRODUCTION

Over the past few years, the lifestyle of people has changed. In this modern era, due to fast lifestyle people are unable to give proper attention to diet, exercise and sleep, which play vital role in our healthy life. In all these conditions, digestive system is the major victim which gets hampered. Nowadays, gastrointestinal problems like indigestion are more common among the general population.

In Ayurveda, there are so many formulations which play important role in gastrointestinal problems and have proven their safety and efficacy. Among them Trikatu[1] choorna is most commonly prescribed by Ayurvedic practitioners for digestive impairment such as Aruchi (anorexia). Trikatu choorna is a poly herbal formulation of three Katu (pungent in taste) dravyas, which consists of the powder form of fruits of Pippali[2] (*Piper longum* Linn.), fruits of Maricha[3] (*Piper nigrum* Linn.), and rhizomes of Shunti[4] (*Zinziber officinale* Linn.) in equal proportion. Trikatu choorna is one of the drug of choice in cases of Agnimandya (decreased digestive fire). In Brihattrayi, it is recommended for various diseases due to Agni (Digestive fire) vitiation such as Grahaniroga, Udara roga (ascitis), Arsharoga (piles) etc. Among the three ingredients of Trikatu choorna Maricha is Laghu (light), Teekshna (tissue penetrating), Ushna (hot), Ruksha (dry) in guna (nature).[5] Maricha (Black Pepper) consists of fully mature dried fruit of *Piper nigrum* Linn. Belonging to Piperaceae family. All contents of Trikatu are commonly known spices to many traditions. The past studies have proven digestive stimulant activity of spices. So this study is proposed to assess the digestive stimulant activity of Maricha choorna in comparison with Trikatu choorna and to rule out their action on digestive enzymes namely alkaline phosphatase, alpha amylase, lipase and protein content. As Trikatu choorna[6] and Maricha choorna both have Deepana activity, it is interesting to find which among them has better digestive stimulant activity. In the past, clinical study on Trikatu choorna as appetite stimulant was conducted and was found effective for treating Avipak(feeling of indigestion even after taking food in less quantity), Prasek(feeling of excessive salivation), Kshudhamandya, Shirogaurav(feeling of heaviness at head), Amashay Gaurav(feeling of heaviness at epigastric region), Antrakujan(feeling of peristaltic movements even the sounds can be audible), Pravahan(strenuous defecation) and concluded that it is highly effective in treating Agnimandya.[7] But no one had conducted animal study in the past to evaluate digestive stimulant activity of Trikatu choorna. Also the comparison of the same with each of its constituents has not been done before.

Literature Survey

All the available literature in Bruhatrayi and Laghutrayi, alongwith updated Ayurvedic literature upon the digestive action of Maricha and Trikatu was reviewed. Many studies on digestive stimulant activity of various species including Pippali *(Piper longum*), Maricha (*Piper nigrum*), and Shunthi (*Zinziber officinale*) have been done in the past. Annamalai et al have conducted study on the effects of Trikatu choorna and its individual components on the gastro-intestinal tract and have come to the conclusion that the contents of Trikatu increases the rate of absorption and gastric pH, while delaying the gastric emptying time. Krishnapura Srinivasan[8] has conducted a study on the influence of dietary spices and their active principles on digestive enzymes of small intestinal mucosa of rats and has concluded that the spices tend to increase the activity of lipase, amylase and other digestive enzymes and also there is a significant increase in the secretion of bile. K. Platel and Srinivasan[9] have also conducted experiments on the activity of spices on the digestive enzymes of rat pancreas and small intestinal mucosa and have come to the same conclusion that spices tend to improve and accelerate digestive enzyme activity.

Study Rationale

Trikatu choorna is a well-known digestive stimulant, used primarily for its Lekhan(anti-obesity), Deepan and Pachan properties. The use of Maricha alone vs the use of Trikatu (i.e Maricha in combination with Pippali and Shunthi) must be compared to find the efficacy of the single drug and also to justify the use of the combination drug.

Out of the three drugs – Shunthi is easily available and economically more affordable to the common man than the other two spices. The use of one drug alone, than the use of combination is hence much more preferable economically. If one drug has proven grossly better result as a digestive stimulant or even if the specificity of one drug towards the digestion of one specific food element, for eg: Lipid is digested better by one drug alone than in combination, then clinically such methods can be adopted to ensure the use of minimal drug with maximum result.

Animal study has been undertaken to get an unbiased result with more parameters that can be taken into consideration, which in a clinical trial would not have been possible considering the difference in body structure and hunger of each individual.

Methodology: The study was carried out in the following manner.

Collection and verification of Raw drugs

The dry seeds of Maricha were purchased from Dr. Balasaheb Sawant Konkan Krishi Vidyapeeth, Dapoli. Pippali was purchased from 'Manakarnika Pharmacy, Pune'. As per mentioned in Ayurvedic classic texts that Pippali should be used for medicinal purpose only after storing them for over one year (puran Pippali), The Pippali was then allowed to dry completely for the period of one year. Sunthi was purchased from Satara. All the above three raw drugs were sent for authentication.

Preparation of choorna: Trikatu choorna and Maricha choorna were prepared as per the procedure given in the Ayurvedic Formulary of India.[10]

Maricha choorna: Dry seeds of Maricha were grounded in the mixer to get fine powder and passed through 85 number mesh.

Trikatu choorna: All the three ingredients of Trikatu choorna (Sunthi, Maricha, Pippali) were grounded in the mixer separately to get fine powder and passed through 85 number mesh. Then all the three choornas were taken in same quantity and mixed together to get uniformly blended Trikatu choorna.

Standardisation of Trikatu Choorna and Maricha Choorna: After preparation of choorna, all the choornas were sent for standardisation and correlated with standards mentioned in API.[11]

Experimental study

Sprague Dawley Rats, females of body weight ranging 150-220 gms were selected for this study.

They were divided into 4 groups namely – Normal group, Vehicle Control group, Test drug 1 (Maricha Choorna) Group, Test drug 2 (Trikatu Choorna) Group. In each groups 6 animals were taken.

In general, Choorna kalpana dosage told by Sharangadhara is one karsha (12gms).[12] But this dosage is not for all types of patients, it is told for Balvaan (possessing proper health) patient. For Alpa Bala person it should be one tanka and can be increased further. As both Trikatu choorna and Maricha choorna are Teekshna, it is advised to be administered at half the general dose i.e. 6gms.[13] So after applying Paget and Barnes equation for calculation of

animal dosage it was fixed at 540mg/kg of rats. As it was given in two divided dosage daily i.e. 540/2 = 270mg every time. The dosage was hence fixed at 300 mg/ kg of rats for ease of dosaging and calculation of each dose. Toxicity studies done in the past, shows that our dosage does not cause any adverse effect on rats.

As both Trikatu and Maricha both are poorly dissolvable in water, Carboxymethyl cellulose was used as the vehicle for making the suspension of Pippali and Trikatu Choorna. Standard CMC Sodium salt was taken and triturated with distilled water until a clear solution was obtained. The test drugs were then made into suspension with CMC with the concentration being 100 mg of test drug per 1ml of dose.

On the basis of Ayurvedic reference mentioned by Acharya Sushrut - that a drug should be given for atleast seven days to conclude it's result,[14] so the seven day trial was conducted. Each group was fed with normal basal diet and allowed to take free food and water supply. The drug was given to the respective group twice daily, first at 10 am and other at 4 pm.

Dosing Schedule

1. To the normal group, standard pellets were administered regularly for 7 days.
2. To the Vehicle control group. Calculated dose of CMC was administered orally for 7 days along with standard diet.
3. To the test group of Maricha choorna calculated "x" dose of Maricha choorna was given orally for 7 days along with standard diet
4. To the test group of Trikatu choorna calculated "x" dose of Trikatu choorna was given orally for 7 days along with standard diet.

To assess the hunger criteria, food intake of animals of each group was calculated for each day.

We have chosen the enzyme analysis method to evaluate the digestive stimulant activity and the enzyme estimation was done at the end of 7 days of experimental trial and after overnight fasting. On 8th day, for the serum enzyme evaluation, the blood samples of each animals of each groups were collected under light ether anaesthesia. These samples were allowed to settle down and subsequently centrifuged to obtain clear serum. After that, the rats were sacrificed under light ether anaesthesia. Then the animals were dissected and intestines were

flushed with ice cold 0.9% saline. The entire length of intestines leaving 5cms below and above were dissected and the mucosal scrapings were obtained.

The mucosal scrapings of each animals were collected in tubes separately and centrifuged with 0.5 ml of 0.9% normal saline to obtain homogenous mixture. Then samples were tested for the enzyme estimation. Then both the samples collected from intestinal mucosa and serum were tested for enzyme estimation with the help of standard enzyme estimation kits bought from Delta company.

RESULTS

Table 1.1: The food intake in gms was measured for each day of the experimentation.

Group	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Normal	72	60	66	70	57	68	65
Control	54	61	96	84	33	60	53
Test 1	82	84	90	92	94	80	78
Test 2	74	72	82	84	90	78	75

Enzyme levels in Intestinal Mucosa.

Groups	Alkaline Phosphatase (U/L)	Alpha Amylase (U/L)	Lipase (U/L)	Protein Content (g/dl)
Normal	35.18 ± 13.25	34.04667 ± 4.713652	617.07 ± 110.8278	2.7 ± 0.051928
Control (CMC)	167.59 ± 37.66	21.22 ± 3.903374	903.85 ± 162.111	2.550167 ± 0.059693
Test drug I (Maricha)	103.64 ± 80.45	28.49283 ± 8.627573	1052.383 ± 130.502	2.666333 ± 0.058435
Test drug II (Trikatu)	315.58 ± 154.89	19.77983 ± 7.643729	876.30 ± 94.65013	2.7395 ± 0.079232

Serum Enzyme levels.

Groups	Alkaline Phosphatase (U/L)	Alpha Amylase (U/L)	Lipase (U/L)	Protein Content (g/dl)
Normal	233.22 ± 25.666	442.22 ± 69.782	13.07 ± 1.0797	7.522 ± 0.1584
Control	203 ± 23.883	410.43 ± 76.549	6.65 ± 0.4956	7.838 ± 0.1667
Test drug I	176.47 ± 14.501	360.66 ± 100.59	8.6513 ± 1.5327	10.564 ± 0.6784
Test drug II	389.35 ± 61.865	60.662 ± 14.63	8.3568 ± 0.678	9.7773 ± 0.4915

GRAPHICAL PRESENTATION OF OBSERVATION AND RESULTS OF EXPERIMENTAL STUDY

INTESTINAL MUCOSAL ENZYMES

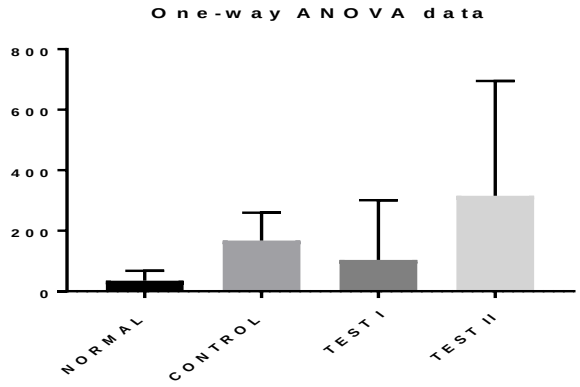

Figure 1: Alkaline phosphatase in intestinal mucosa.

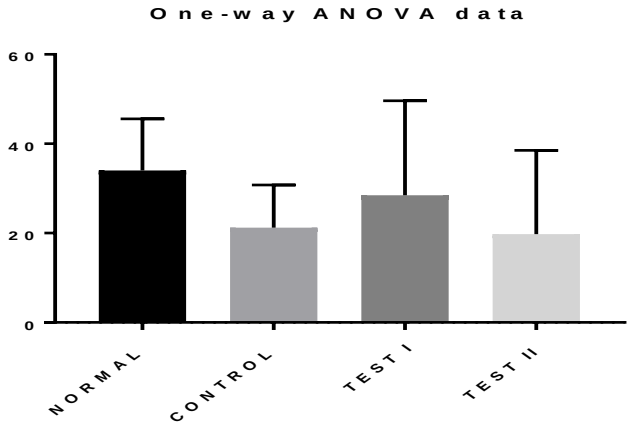

Figure 2: Alpha Amylase in intestinal mucosa.

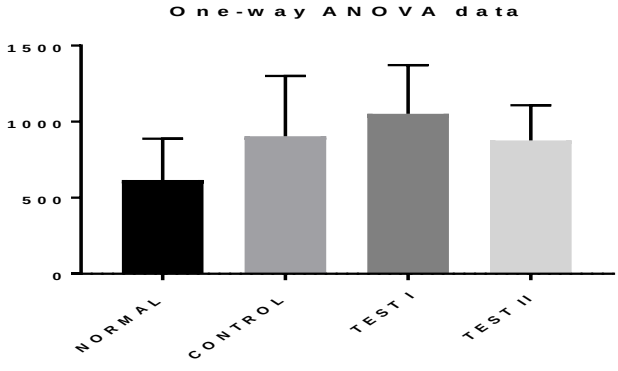

Figure 3: Lipase in intestinal mucosa.

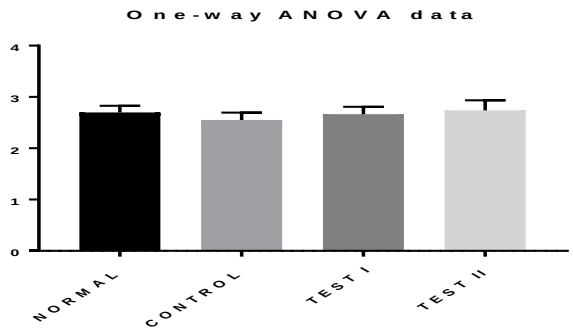

Figure 4: Total Protein content in intestinal mucosa.

SERUM ENZYMES

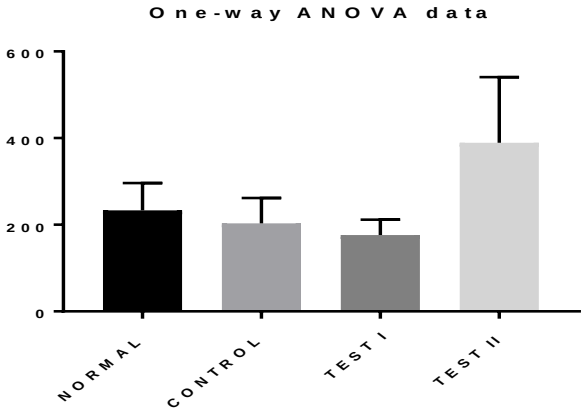

Figure 5: Effect of Maricha Choorna and Trikatu Choorna on alkaline phosphatase enzyme level in serum.

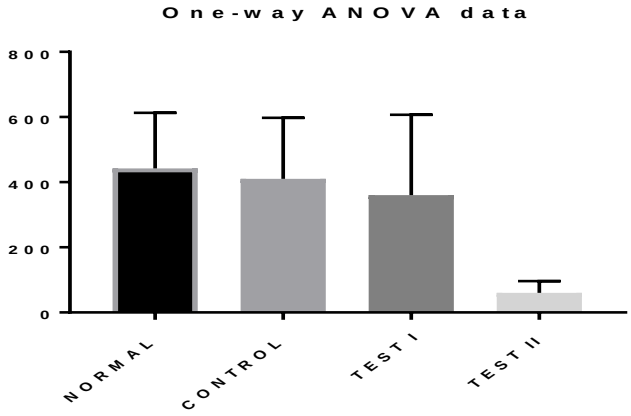

Figure 6: Effect of Maricha Choorna and Trikatu Choorna on alpha amylase enzyme level in serum.

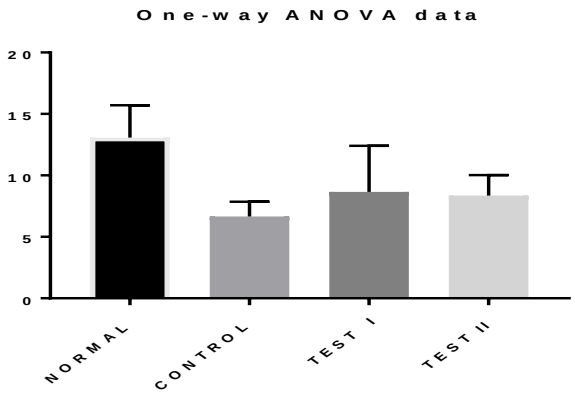

Figure 7: Effect of Maricha Choorna and Trikatu Choorna on lipase enzyme level in serum.

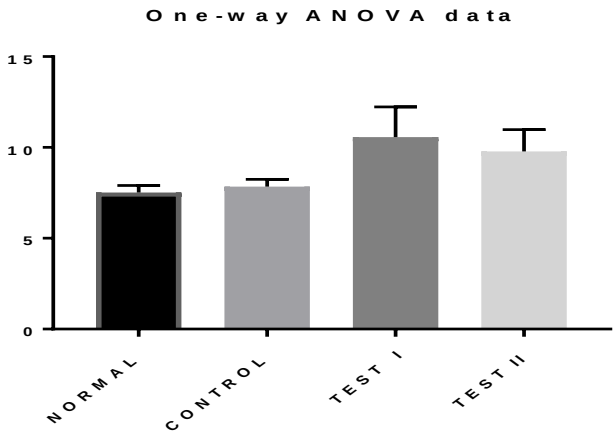

Figure 8: Effect of Maricha Choorna and Trikatu Choorna on protein content level in serum.

DISCUSSION

The present study titled **"A comparative study of digestive stimulant action of Maricha choorna and Trikatu choorna in experimental rats"**, was undertaken to evaluate digestive stimulant activity of Maricha choorna in comparison with that of Trikatu choorna**.**

The present study was conducted to evaluate the digestive stimulant activity of both Trikatu Choorna and Maricha choorna as both the drugs have been mentioned for their Deepana activity in Ayurvedic literature. In the present study to assess the digestive stimulant activity the pancreatic enzymes are taken as parameters also the serum values of these enzymes are taken into consideration.

To assess the hunger criteria, food intake of animals of each group was calculated for each day, which showed that there was increase in food intake in both groups receiving test drugs upto the fifth day, but thereafter it decreased steadily for the next two days. It might be due to Teekshna property of both drugs i.e. they may have slight irritating effect on intestinal mucosa. From this we can conclude that for the expected Deepana result, both the drugs should be given upto maximum 5 days and its excessive usage should be avoided.

Alkaline phosphatase level (ALP)

Statistically data obtained from intestinal mucosa does not show significant increase in the enzyme level (i.e. $p>0.05$).

But when the mean values of each enzymes are taken into consideration, the following inferences can be drawn.

Huge variations in the enzyme values were seen when it was compared with normal group values.

Though there was no significant increase in the alkaline phosphatase level of intestinal mucosa but its trend shows increased ALP level as compared to normal group. There was approximately nine times increase in the ALP levels of Trikatu treated group i.e. Test II group as compared to normal group and approximately 3 times increase in Maricha treated group i. e. Test I group as compared to normal group.

The serum ALP values show significant increase in the ALP values of Trikatu choorna treated group but there is no significant increase in ALP values of Maricha choorna treated group.

So the data shows that Trikatu significantly increases ALP values in comparison with Normal, Control and Maricha group.

It indicates that both the drugs are having definite action on the hepatobilliary system as per their values in intestinal mucosa and blood serum. But it is clear that Trikatu is having better stimulating action on ALP values.

So the ALP values of Trikatu choorna fed group indicates that it has definite action on the hepato biliary system, as per the production of ALP in intestinal mucosa and serum values

and the increased values are not indicative of any pathological condition but it is indicative of stimulatory effect of Trikatu on ALP-digestive enzyme.

Maricha group also shows increased ALP values as compared to normal but lesser than Trikatu group. Past studies[15] have shown that Maricha as a spice and it increases biliary bile acid secretion when administrated orally. So it is definitely useful in obstructive pathology because of its Teekshna guna and Hot potency.

Amylase

Statistically there is no significant increase in alpha amylase level in mucosal samples. The intestinal mucosal amylase values for Maricha group are within normal range. Also Trikatu group does not show any significant increase in alpha amylase level. But its trend shows approximately 42% decrease in alpha amylase level in Trikatu group when compared to normal group.

Trikatu group also shows significant decrease in serum alpha amylase values. And also significantly decreased alpha amylase in comparison with Maricha group. There is about 18% decrease in alpha amylase level from normal group in Maricha choorna group and 86% decrease from normal group in Trikatu choorna group. So Trikatu significantly decreases alpha amylase levels in serum (at $p<0.01$). Trikatu significantly decreases alpha amylase levels as compared to Maricha group (at $p<0.05$).

Pancreatic juice that contains alpha amylase is released into the duodenum when a meal is present in the digestive tract. Pancreatic amylase continues digestion of starch and glycogen in the small intestine. Alpha amylase act at neutral or slightly alkanine pH values.[16]

Increased alpha amylase levels in humans are found in pancreatitis-because of damage to the cells that produce amylase. Total amylase readings of over 10 times the upper limit of normal (ULN) are suggestive of pancreatitis.

As our results show decrease in alpha amylase level in both test drugs, surely there is no evidence of pancreatitis.

Lipase

Pancreatic lipase is secreted into the duodenum through the duct system of the pancreas. Its concentration in serum is normally very low. Under extreme disruption of pancreatic

function, such as pancreatitis or pancreatic adenocarcinoma, the pancreas may begin to autolyse and release pancreatic enzymes including pancreatic lipase into serum concentration of pancreatic lipase, acute pancreatitis can be diagnosed.

The present study shows statistically there was no significant increase seen in mucosal values of both test drug groups. But their values show difference when compared with normal group. Mean Mucosal estimates show an elevated secretion of Pancreatic lipase in the lumen of the test I and test II groups.

Higher serum lipase value was seen in Maricha group as compared to Trikatu group. There is about 42% increase in lipase seen in the Test drug 2 i.e. Trikatu choorna and 70% increase in the Test drug 1 i.e. Maricha choorna group. Also 46% increase in the Control group CMC.

So the overall data tends to show that Maricha is having better action than Trikatu, normal and control group in fat digestion. It is more lipolytic than Trikatu.

Trikatu choorna group shows higher secretion of pancreatic lipase in the lumen which is clearly seen in the mucosal estimate. But when the values are compared with Maricha group, it shows about two times increased lipase secretions as compared to Trikatu group.

This data is indicative that there is stimulation of pancreatic lipase in the lumen seen in all three groups. And the low serum values are indicative of they are less released in blood stream.

Lipase values of Trikatu found slightly lesser than that of Maricha choorna. It means Maricha choorna is more effective in fat digestion.

Amylase and Lipase

When dietary fat is substituted in food, it is often seen that it leads to the excessive secretion of lipase which helps in fat digestion and it consequently causes decrease in the production of amylase as well as its transport. In our study also we found relative lower values of amylase in both intestinal lumen and serum in both test groups, more specifically in Trikatu group.

As our both test drugs have decreased the serum amylase and lipase values. So definitely there is no evidence of acute pancreatitis.

Trikatu is combination of three spice mixes, namely Pippali, Maricha and Shunthi. Trikatu is hot in potency and having deepana activity. Its contents Maricha, Pippali and Sunthi all are having hot potency. Trikatu helps in alleviation of Kapha and Vata dosha but increases Pitta dosha. Its ingredients both Pippali and Maricha are Teekshna in property. Shunthi is having Madhura Vipaka and Grahi activity. So the use of Trikatu should be done according to Prakruti, Bala, Kala and Dosha of patient. Though it is mentioned in the literature that all ingredients should be taken into equal amount, we can adjust their quantity according to patient and desired results. If we want more lipolytic activity, we can add more amount of Maricha choorna in the combination or single Maricha choorna can be given to the patient. Kaal means period upto which both the choornas to be given, should be fixed on their properties. Because it may show adverse effect or inflammatory changes due to their Teekshna and Hot potency. So all these things should be taken into consideration.

Hence the present study showed that the lipolytic action of Maricha Choorna was better than Trikatu Choorna. Both the choornas are more helpful in fat digestion than in carbohydrate digestion. Thus in clinical practice, where lipid digestion is concerned the use of Maricha choorna over Trikatu choorna must be done.

CONCLUSION

Maricha choorna and Trikatu choorna have definitive stimulatory action on digestive enzymes and thereby on pancreas and the hepato-biliary system.Trikatu choorna shows more stimulatory effect on alkaline phosphatase enzyme as compared to Maricha choorna. While Maricha choorna shows more stimulatory effect on lipase enzyme as compared to Trikatu choorna.The results show that Maricha is having more lipolytic activity than Trikatu. It is more useful in fat digestion than Trikatu. Maricha is mainly useful in[17] obstructive pathology due to its Pramathi[18] and Chedana property.

As Maricha choorna as a solo has potential to digest lipids more effectively than Trikatu choorna so where fat digestion is accepted more we can use only Maricha choorna instead of Trikatu choorna for better results.

Maricha and Trikatu are both are Teekshna dravyas. So these should be used in patients according to their Prakruti and Dosha status. These should be used very cautiously in Pitta Prakruti patients. Trikatu choorna and Maricha choorna both the drugs have negligible effect on Carbohydrate digestion as there is no such stimulatory effect on amylase enzyme. Hence

Maricha choorna must be used where digestion of fat is concerned which gives better results as compared to Trikatu choorna.

Scope of further study

- The other digestive enzymes which were not studied in this experiment can also be tested like tripsin, chemotrypsin etc.
- Also the effect of both Trikatu and Maricha choorna on biliary flow must be tested.
- Instead of taking Trikatu choorna as per ayurvedic text, we can try the study on Trikatu choorna with different proportions of its constituents to check its digestive stimulant activity.
- Histopathology of the organs involved in digestion after the trial completion –specifically the pancreas and hepato-biliary system must be carried out.
- The another study with less duration like upto 5 days should be carried out to see the digestive stimulant effect.
- Each day enzyme estimation should be carried out to see proper effect of choornas on digestive enzymes on every day basis like on first day, second day and so on.

REFERENCES

1. Shri Govinda Das, Bhaishajya Ratnavali, Edited by Shri Ambikadatta Shastri, Chaukhamba Prakshan, Varanasi, Paribhasha Prakarana-19, 2011; 50.
2. Bhav Mishra, Bhavaprakash Nighantu, Prof. Krishnachandra Chunekar, Haritakyadi Varga, Chaukhamba Bharti Academy, Varanasi, Revised Edition 2010, Shlok no 53-58, 15.
3. Acharya Bhavamishra, Bhavaprakash Nighantu, Edited by Prof. Krishnachanda Chunekar, Haritakyadi Varga- 62-63, Chaukhamba Prakashan, Varanasi, 2011; 18.
4. Bhav Mishra, Bhavaprakash Nighantu, Prof. Krishnachandra Chunekar, Haritakyadi Varga, Chaukhamba Bharti Academy, Varanasi, Revised Edition 2010, Shlok no 44-48, 12.
5. Acharya Bhavamishra, Bhavaprakash Nighantu, Edited by Prof. Krishnachanda Chunekar, Haritakyadi Varga- 62-63, Chaukhamba Prakashan, Varanasi, 2011; 18.
6. Acharya Sharangdhar, Sharangdhar Samhita, Bhishak Aadhamalla virachit 'Deepika'- Pandit Kashiram Vaidya Virachit- 'Gudharthdeepika', Vidyasagar Pandit Parshuram Shastri, Chaukhamba Publications, 2013, Chapter 6, Shlok nos.-9-12.

7. Singh A,K., Clinical evaluation of Trikatu as appetite stimulant(Agnivardhan), Journal of Pharmaceutical and Scientific Evolution, 2012.
8. Platel K., Srinivasan K., Influence of Dietary spices and their active principles on digestive enzymes of small intestinal mucosa in rats, 1996.
9. Platel K., Srinivasan K., Influence of Dietary spices and their active principles on pancreatic digestive enzymes in albino rats, 2000.
10. Ayurvedic Formulary of India part I, second edition, Government of India, Ministry of Health and Family Welfare, Department of Indian Systems of Medicine and Homeopathy, The Controller of Publications Civil lines, New Delhi, Second edition, 2003.
11. The Ayurvedic Pharmacopoeia of India, (API), Government of India, Department of AYUSH, Part 1, 1st Edition, The controller of publication, Civil lines, New Delhi, 2001; 3: 111.
12. Acharya Sharangadhara, Sharangadhara Samhita, Edited by Brahmananda Tripathi Madhyam khanda-6/1, Chaukhamba Surabharati Prakashana, Varanasi, 2011.
13. Pandita Sarngadharacharya, Sarngadhara-Samhita, Annotation with Hindi Commentary "Dipika", Dr. Brahmanand Tripathi, Madhyam khand, Chaukhambha Surbharti Prakashan, Varanasi, 2011, Chapter 2, shlok no 154.
14. Acharya Sushruta, Sushruta Samhita, Edited by Dr. Anant Ram Sharma, part I, Sutrasthana 35/49, Dalhana commentary, chaukhamba Surbharati prakashana, 2013; 283.
15. Srinivasan K. Black pepper and its pungent principle-piperine. A review of diverse physiological effects. Crit. Rev. Food Sci. Nutr 2007; 47: 735-748.
16. Margaret E., Smith Ph D. Dsc. Et al, Digestion and absorption, digestive system, second edition, 2010.
17. Acharya Charak, Charak Samhita, Edited by Dr.Brahmanand Tripathi, sutrasthana 27/298, Chaukhamba Surbharti Prakashan, Varanasi, 2009; 537.
18. Acharya Sharangadhara, Sharangadhara Samhita, Edited by Brahmananda Tripathi Madhyam khanda-6/1, Chaukhamba Surabharati Prakashana, Varanasi, 2011.