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MARKER BASED ANALYTICAL STUDIES ON *RASAM*: A SOUTH INDIAN TRADITIONAL FUNCTIONAL FOOD

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ABSTRACT

Rasam, is a traditional functional food as its ingredients are medicinally claimed for various ailments. The main spices used in the preparation of *rasam* are tamarind, turmeric, chili pepper, cumin, garlic, black pepper, black mustard, curry leaves, coriander and asafoetida. Exhaustive literatures are available for the ingredients used in the preparation of *rasam*, but the details of chemical and/or biological markers present in *rasam* were not available. Hence, this study was carried out to investigate a marker based analytical study on *rasam* in a stage wise samples (RS3 and RS4). Marker compounds like, β-sitosterol, ascorbic acid, capsaicin, curcuminoids, ferulic acid, mahanimbine, piperine and quercetin were analysed for their presence by HPTLC/HPLC in *rasam*. The marker analytic study of *rasam* samples RS3 and RS4 showed only the presence of ascorbic acid, capsaicin, ferulic acid and piperine. Furthermore, the study indicated that increase in temperature from RS3 to RS4 decreased the quantity of capsaicin and piperine whereas, the quantity of ascorbic acid increased from RS3 to RS4 in *rasam*. Ferulic acid remained almost unchanged from RS3 to RS4. Further studies are needed to accurately ascertain the exact chemical composition of *rasam* apart from the markers studied.

KEYWORDS: *Chaaru*, HPLC, HPTLC, *Saaru*, spices.

INTRODUCTION

Rasam, is a common South Indian traditional spice soup. It is also called as *chaaru* or *saaru* in different South Indian languages. In a traditional South Indian meal, it is preceded by a *sambar* rice course and is followed by curd rice. The main spices used in the preparation of *rasam* are tamarind, turmeric, chili pepper, cumin, garlic, black pepper, black mustard, curry leaves, coriander and asafoetida.[1] *Rasam*, is a traditional functional food as its ingredients are medicinally claimed for various ailments. In South India, it is considered as an effective home remedy for common cold, cough and an antidote for flu or fever.[2,3] Devi and Priyadharshini, 2014 have reported that *rasam* is traditionally used for the treatment of cold, cough and diabetes.[4] Mani et al., 1997 have reported that the glycemic index (GI) and the triacyglycerol response in ninety normal volunteers after consuming South Indian meals with *rasam* significantly controlled diabetes.[5] Bolla et al., 2015 have reported that South Indian diet with *rasam* everyday showed a significant reduce in the blood sugar levels of 40 volunteers between 30 and 60 years.[6] Rajan et al., 2001 have reported that *rasam* is given daily in the evening to nursing mothers for inducing more secretion of milk.[7] *Rasam* has also been reported for anti-microbial[8] and anti-platelet activity.[9] Exhaustive literatures are available for the ingredients used in the preparation of *rasam*, but the details of chemical and/or biological markers present in *rasam* were not available. Hence, this study was carried out to investigate a marker based analytical study on *rasam*.

MATERIALS AND METHODS

Materials

All ingredients of *rasam* were purchased from Arokya organic shop, Vellore, Tamil Nadu. All utensils used for the preparation of *rasam* were of Stainless Steel 316 grade (SS 316). All other chemicals and solvents were obtained from SD Fine Chemicals (Mumbai, India) and were of analytical grade. All marker compounds studied like, β-sitosterol, ascorbic acid, capsaicin, curcuminoids, ferulic acid, mahanimbine, piperine and quercetin were from Natural Remedies Pvt Ltd, Bengaluru, Karnataka.

Preparation of *rasam*

Rasam was prepared in a stage wise manner as mentioned below:

1. Tamarind fruit pulp mixture (T1): 6.88 g of tamarind fruit pulp was immersed in 450 mL of water for 10 min, then it was hand crushed for 45 times and strained. The strained

liquid was rinsed with 5 mL water, to which 0.4 g of turmeric powder and 4 g of sea salt was added.

2. Tomato fruit mixture (T2): 82.44 g of fresh tomato fruits were cut and hand crushed for 60 times. The crushed fruit was rinsed with 5 mL of water.
3. Spice mixture (T3): 1.33 g of pepper drupes was crushed in a SS 316 mortar and pestle for 85 times. 2.67 g of cumin fruits was added over to the crushed pepper drupes and crushed for 100 times. To the above crushed mixture 0.82 g of chili pepper was added and crushed for 50 times. To the above mixture 9.63 g of garlic cloves was added and crushed for 90 times.
4. All mixture (T4): Tomato fruit mixture (T2) was rinsed with 10 mL of water and spice mixture (T3) was rinsed with 10 mL of water. Both rinsing were added to tamarind fruit pulp mixture (T1).
5. Final product (T5): 4 ml of Indian sesame oil was heated at 60 °C for 2 min. After 5 seconds 0.82 g of mustard seeds were added. After 3 seconds 1.53 g of whole chili pepper was added. After 2 seconds 0.61 g of curry leaves was added. Immediately all mixture (T4) was rinsed with 20 mL of water and added. The whole liquid was allowed to boil for a 5 min. After 5 min 1.50 g of coriander leaves was added, this was designated as sample RS3. When the liquid frothed, 0.05 g of asafoetida was added and the heating was switched off to yield the final product, this was designated as sample RS4.

The stage wise samples RS3 and RS4 of *rasam* were used for further studies.

High Performance Thin Layer Chromatography (HPTLC) equipment

A Camag TLC system equipped with Camag Linomat V an automatic TLC sample spotter, Camag glass twin trough chamber (20 X 10 cm) were used for the analysis. Chromatography was performed using pre-activated (60 °C for 5 min) silica gel $60F_{254}$ TLC plates (20 X 10 cm; layer thickness 250 µm). Samples (RS3 and RS4) and standard was applied on the plate as 8 mm wide bands with an automatic TLC sampler under a flow of N_2 gas, 10 mm from the bottom and 10 mm from the side and the space between two spots were 15 mm of the plate. The linear ascending development was carried out in a Camag twin trough chamber saturated with 20 mL mobile phase for 20 min at room temperature (25±2 °C and 40% relative humidity). 5 µL of the sample solution was applied in on the TLC plate and developed with mobile phase toluene: ethyl acetate (9:1, v/v). The plates were developed up to 8 cm under chamber saturation conditions. Subsequently to the development, TLC plates were dried in

current air with the help of a hair dryer. The post chromatographic derivatization was carried out with anisaldehyde-sulphuric acid placed in a dipping chamber (CAMAG) followed by heating in an oven at 100 °C for 5–10 min.[10]

High Pressure Liquid Chromatography (HPLC) equipment

Shimadzu integrated liquid chromatographic system LC/2014 comprising of system controller unit, degassing unit, low pressure isocratic unit, two solvents pump unit, mixer, auto sampler, column oven, UV - Vis detector and class VP ver 6.0 work station were used for analysis.

β-sitosterol

β-sitosterol was analysed in *rasam* samples RS3 and RS4 by HPTLC. The experimental condition was as mentioned above in HPTLC equipment section.

Ascorbic acid

Ascorbic acid was analysed in *rasam* samples RS3 and RS4 by HPLC. A 5 µm pore size Zorbax SB RP C18 column with a gradient elution prepared from 0.1% (v/v) acetic acid in HPLC-grade water and methanol was used. The flow rate was 0.9 mL/min and detected at 242 nm.

Capsaicin

Capsaicin was analysed in *rasam* samples RS3 and RS4 by HPLC. A Betasil C18 column (particle size 3 µm, dimension 150 X 4.6 mm) with an isocratic mobile phase of water-acetonitrile at 50:50 (v/v) was used. The flow rate was 1.5 mL/min and detected at 278 nm.

Curcuminoids

Curcuminoids (bisdemethoxycurcumin, demethoxycurcumin and curcumin) were analysed in *rasam* samples RS3 and RS4 by HPLC. A Luna C18 column (particle size 5 µm, dimension 250 X 4.6 mm) with an isocratic mobile phase of acetonitrile and 10 mM Na_2HPO_4–H_3PO_4 (pH 5.0) with a proportion of 50:50 (v/v) was used. The flow rate was 1.0 mL/min and detected at 420 nm.

Ferulic acid

Ferulic acid was analysed in *rasam* samples RS3 and RS4 by HPLC. A RP HiQSil C18 column (particle size 5 µm, dimension 250 X 4.6 mm) with an isocratic mobile phase of

acetonitrile and 10% acetic acid (20:80, v/v) was used. The flow rate was 1.0 mL/min and detected at 280 nm.

Mahanimbine

Mahanimbine was analysed in *rasam* samples RS3 and RS4 by HPLC. A Luna C18 column (particle size 5 µm, dimension 250 X 4.6 mm) with an isocratic mobile phase of methanol and 0.5% acetic acid in water (90:10, v/v) was used. The flow rate was 1.0 mL/min and detected at 237 nm.

Piperine

Piperine was analysed in *rasam* samples RS3 and RS4 by HPLC. A Luna C18 column (particle size 5 µm, dimension 250 X 4.6 mm) with an isocratic mobile phase of acetonitrile: water: acetic acid (60:39.5:0.5, v/v/v) was used. The flow rate was 1.0 mL/min and detected at 347 nm.

Quercetin

Quercetin was analysed in *rasam* samples RS3 and RS4 by HPLC. A HiQ Sil C18 column (particle size 5 µm, dimension 250 X 4.6 mm) with an isocratic mobile phase of methanol: 0.1% ortho phosphoric acid (65:35, v/v) was used. The flow rate was 1.0 mL/min and detected at 370 nm.

RESULTS AND DISCUSSION

The biological source of the ingredients and its quantity used in the preparation of *rasam* is shown in Table 1.

Table 1: Biological source of the ingredients and its quantity used in the preparation of *rasam*.

Common names	Morphological part used	Nature of the material	Botanical name	Family	Quantity
Tamarind	Ripped fruit pulp	Dried	*Tamarindus indica* L.	Fabaceae	6.00 g
Turmeric	Rhizome powder	Dried	*Curcuma longa* L.	Zingiberaceae	0.40 g
Sea salt	NA	Solid	NA	NA	4 g
Tomato	Ripped fruit	Fresh	*Solanum lycopersicum* L.	Solanaceae	82.44 g
Chili pepper	Crushed fruit of long chilli pepper	Dried	*Capsicum annuum* L.	Solanaceae	0.82 g
Cumin	Ripped fruit	Dried	*Cuminum cyminum* L.	Apiaceae	2.67 g
Garlic	Cloves	Dried	*Allium sativum* L.	Amaryllidaceae	9.63 g
Black pepper	Unripe drupe	Dried	*Piper nigrum* L.	Piperaceae	1.33 g
Indian sesame oil	Seed	Oil	*Sesamum indicum* L.	Pedaliaceae	4 mL
Black mustard	Seed	Dried	*Brassica nigra* L.	Brassicaceae	0.82 g
Chili pepper	Whole fruit of long chili pepper	Dried	*Capsicum annuum* L.	Solanaceae	1.53 g
Curry leaves	Leaves	Fresh	*Murraya koenigii* (L.) Sprengel	Rutaceae	0.61 g
Portable water	NA	Liquid	NA	NA	500 mL
Coriander	Leaves	Fresh	*Coriandrum sativum* L.	Apiaceae	1.50 g
Asafoetida	Dried latex (oleogum resin) exuded from the rhizome or tap root	Powder	*Ferula assa-foetida* L.	Apiaceae	0.05 g

β-sitosterol is one of several phytosterols and a chemical analogue of cholesterol. It is widely distributed in the plant kingdom. β-sitosterol has been reported for a wide array of biological activities. However, it has been stated that "the ubiquitous occurrence of β-sitosterol, plant sterols in general, and their glucosides in all vegetables makes it highly unlikely that they have any drug related properties and many reports on their medicinal properties are based on *in vitro* or unrealistically high *in vivo* doses which make a therapeutic application of these compounds highly unlikely".[11,12] In a way this statement is correct, since sitosterol is not drug in the accepted sense, but rather slow acting essential micronutrients or adaptogens

better considered as minor but nevertheless important cell membrane constituents. Hence, β-sitosterol was chosen as a chemical marker to be analysed in RS3 and RS4. Fig. 1 clearly shows the absence of β-sitosterol in RS3 and RS4. β-sitosterol is hydrophobic in nature and soluble in alcohols. The processing in the preparation of *rasam* involves a large quantity of water (500 mL) and only 4 mL of hydrophobic phase (Indian sesame oil), which may be the reason for its absence in RS3 and RS4.

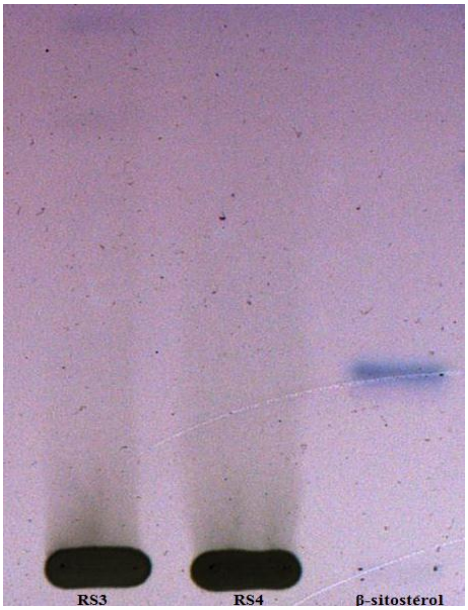

Fig. 1: HPTLC chromatogram showing the absence of β-sitosterol in *rasam* samples RS3 and RS4.

Fig. 2 and 3 shows the HPLC chromatogram of *rasam* samples RS3 and RS4. Ascorbic acid, also known as vitamin C and L-ascorbic acid, is a vitamin found in food and used as a dietary supplement. As a supplement it is used to treat and prevent scurvy.[13] Ascorbic acid has been reported in tamarind, turmeric, tomato, cumin, chili pepper, garlic, mustard and coriander hence, it was studied as both biological and chemical marker in *rasam*. Ascorbic acid is a water soluble vitamin hence, it was identified in both samples RS3 and RS4 (Table 2). Comparatively, RS4 showed almost five times more peak area than RS3 (Table 2).

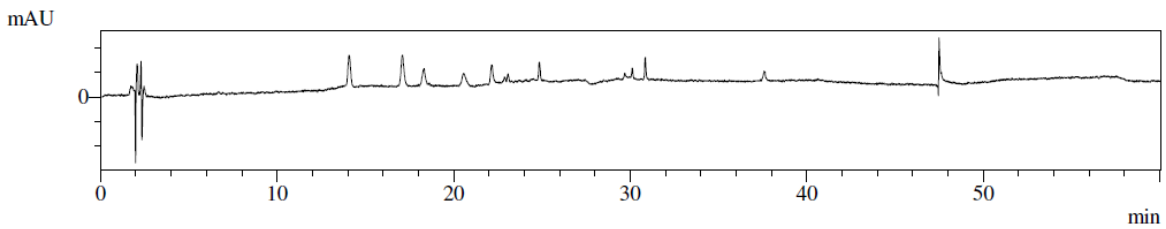

Fig. 2: HPLC chromatogram of RS3.

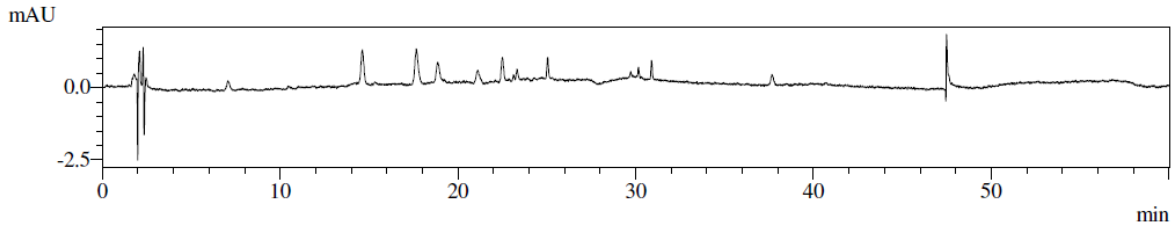

Fig. 3: HPLC chromatogram of RS4.

Capsaicin is an active constituent and the major capsaicinoids of chili pepper. Capsaicin is used as an analgesic in topical ointments, nasal sprays, and dermal patches to relieve pain.[14] It may be applied in cream form for the temporary relief of minor aches and pains of muscles and joints associated with arthritis, backache, strains and sprains, often in compounds with other rubefacients. It is also used to reduce the symptoms of peripheral neuropathy such as post-herpetic neuralgia caused by shingles.[14] Capsaicin transdermal patch for the management of this particular therapeutic indication (pain due to post-herpetic neuralgia) was approved as a therapeutic by the U.S. FDA.[15] Hence, capsaicin was studied as a biological and chemical marker for chili pepper in *rasam*. Solubility of capsaicin in water is 1.3 mg/mL hence, it was identified in both samples RS3 and RS4 (Table 2). Comparatively, RS3 showed higher peak area than RS4 (Table 2). The difference between samples being that RS4 is heated longer than RS3, indicating that an increase in temperature decreases the quantity of capsaicin in *rasam*.

Curcuminoids are the principal constituents of turmeric. It is used as an herbal supplement, cosmetics ingredient, food flavoring, and food coloring. However, most of the reported activities of curcuminoids are based only on *in vitro* and *in vivo* studies. It has yet not been approved for treatment of any human disease.[16] Curcuminoids was studied as a chemical marker for turmeric in *rasam*. Curcuminoids (Bisdemethoxycurcumin, Demethoxycurcumin and Curcumin) are very poorly soluble in water hence, not detected in RS3 and RS4.

Ferulic acid is a hydroxycinnamic acid, a type of organic compound. It is an abundant phenolic phytochemical found in plant cell wall components. Ferulic acid, like many natural phenols, is an antioxidant. Animal studies and in vitro studies suggest that ferulic acid may have direct antitumor activity against breast cancer[17] and liver cancer.[18] Hence, ferulic acid was studied as a biological and chemical marker in *rasam*. Solubility of ferulic acid in water is 780 mg/mL hence, it was identified in both samples RS3 and RS4 (Table 2). Both samples

RS3 and RS4 showed almost equal peak area (Table 2), which shows that change in temperature does not affect the quantity of ferulic acid in *rasam*.

Table 2: Retention time and peak areas of marker compounds in *rasam* samples RS3 and RS4.

Retention time (min)	Peak area	Retention time (min)	Peak area	Retention time (min)	Peak area
Ascorbic acid		**RS3**		**RS4**	
1.758	2455	1.761	451	1.772	2455
Capsaicin		**RS3**		**RS4**	
30.867	443624	30.848	3197	30.886	2710
Bisdemethoxycurcumin		**RS3**		**RS4**	
30.543	23791	ND	NA	ND	NA
Demethoxycurcumin		**RS3**		**RS4**	
30.714	160259	ND	NA	ND	NA
Curcumin		**RS3**		**RS4**	
30.899	848786	ND	NA	ND	NA
Ferulic acid		**RS3**		**RS4**	
15.450	284416	15.457	557	15.461	561
Mahanimbine		**RS3**		**RS4**	
42.180	3869159	ND	NA	ND	NA
Piperine		**RS3**		**RS4**	
30.963	527614.5	30.848	11992	30.891	9190
Quercetin		**RS3**		**RS4**	
26.644	472263	ND	NA	ND	NA

ND-not detected; NA-not applicable.

Mahanimbine is a carbazole alkaloid found in herbs and spices. Acetylcholinesterase inhibition,[19] antidiabetic,[20] hypolipidemic,[20] and anti-oxidant activity[21] has been reported. Mahanimbine has also been reported to alleviate HFD-induced metabolic alterations.[22] Mahanimbine has been reported from curry leaves,[21] hence it was studied as a biological and chemical marker for curry leaves in *rasam*. Mahanimbine being poorly soluble in water was not detected in samples RS3 and RS4.

Piperine is a piperidine alkaloid, along with its isomer chavicine is responsible for the pungency of black pepper. Piperine is under study for a variety of possible physiological effects[23] but the mechanisms of activity for piperine in the human body remain unknown. Piperine is being studied for its potential to affect bioavailability of other compounds in dietary supplements. Piperine increases the absorption of selenium, Vitamin B12, β-carotene, and curcumin, as well as other compounds.[24] Piperine is shown to possess bioavailability-enhancing activity with various structurally and therapeutically diverse

drugs.[25] Hence piperine was studied as biological and chemical marker for pepper in *rasam*. Solubility of piperine in water is 40 mg/mL hence, it was identified in both samples RS3 and RS4 (Table 2). Comparatively, RS3 showed higher peak area than RS4 (Table 2). The difference between samples being that RS4 is heated longer than RS3, indicating that an increase in temperature decreases the quantity of piperine in *rasam*.

Quercetin is a flavonoid widely distributed in nature and the most abundant dietary flavonoid. Quercetin has been reported to inhibit the oxidation of other molecules and hence is classified as an antioxidant.[26,27] Quercetin has been studied for the treatment of cancer and various other diseases, there is no evidence that quercetin (via supplements or in food) is useful to treat cancer or any disease.[28,29] Hence, quercetin was studied as a chemical marker in *rasam*. Quercetin being insoluble in water was not detected in samples RS3 and RS4.

CONCLUSION

Even though many medicinally claimed ingredients were used in the preparation of *rasam*, the marker analytic study of *rasam* samples RS3 and RS4 showed only the presence of ascorbic acid, capsaicin, ferulic acid and piperine. Furthermore, the study indicated that increase in temperature from RS3 to RS4 decreased the quantity of capsaicin and piperine whereas, the quantity of ascorbic acid increased from RS3 to RS4 in *rasam*. Ferulic acid remained almost unchanged from RS3 to RS4. Further studies are required to accurately ascertain the exact chemical composition of *rasam* apart from the markers studied.

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REFERENCES

1. Srinivasan K. Spices as influences of body metabolism; an overview of three decades of research. Food Res Int, 2005; 38(1): 77-86.
2. Parthasarathy VA, Chempakam B, Zachariah TJ, editors. Chemistry of spices. 1st ed. Oxfordshire; CAB International, 2008.
3. Sanmugam D, Kasinathan S. Indian heritage cooking. Singapore; Marshall Cavendish International Asia Pvt Ltd, 2011.
4. Devi KK, Priyadharshini VP. Exploration of nutrient content of traditional recipes of Tamil Nadu with therapeutic properties. Int J Res Appl Nat Soc Sci, 2014; 2(10): 1-12.

5. Mani UV, Mani IU, Iyer UM, Prakash B, Manivannan T, Campbell S et al. Glycemic and lipemic response to various regional meals and South Indian snacks. Int J Diab Dev Countries, 1997; 17: 75-81.
6. Bolla K, Santhi KV, Afnan KS, Veni PK, Kusuma M. Effect of diet counseling on type 2 diabetes mellitus. Int J Sci & Tech Res, 2015; 4(8): 112-118.
7. Rajan S, Baburaj DS, Sethuraman M, Parimala S. Stem and stem bark used medicinally by the tribals Irulas and Paniyas of Nilgiri district, Tamil Nadu. J Nat Rem, 2001; 1(1): 49-54.
8. Agilandeswari D, Mohan Maruga Raja MK. Anti-microbial studies on *rasam*: a south Indian traditional functional food. World J Pharm Res, 2017; 6(5): 766-774.
9. Agilandeswari D, Mohan Maruga Raja MK. Anti-platelet aggregation study on *rasam*: a south Indian traditional functional food. Indo Am J Pharm Res, 2017; 7(4): 8134-8139.
10. Wagner H, Bladt S. Plant Drug Analysis. Berlin; Springer, 1996.
11. Marles RJ, Farnsworth NR. Plants as a source of antidiabetic agents. Econ Med Plant Res, 1994; 6: 149-187.
12. Marles RJ, Farnsworth NR. Antidiabetic plants and their active constituents. Phytomed, 1995; 2: 137-189.
13. American Hospital Formulary Service drug information. In McEvoy GK (eds.). Ascorbic Acid. Bethesda, MD: American Society of Health-Systems Pharmacists, 2007: 3631-3634.
14. Fattori V, Hohmann MS, Rossaneis AC, Pinho-Ribeiro FA, Verri WA. Capsaicin: current understanding of its mechanisms and therapy of pain and other pre-clinical and clinical uses. Molecules, 2016; 21(7): E844.
15. Jones VM, Moore KA, Peterson DM. Capsaicin 8% topical patch (Qutenza)--a review of the evidence. J Pain Palliat Care Pharmacother, 2011; 25(1): 32-41.
16. Gupta SC, Patchva S, Koh W, Aggarwal BB. Discovery of curcumin, a component of the golden spice, and its miraculous biological activities. Clin Exp Pharmacol Physiol, 2012; 39(3): 283–299.
17. Saulnier L, Thibault JF. Ferulic acid and diferulic acids as components of sugar-beet pectins and maize bran heteroxylans. J Sci Food Agri, 1999; 79(3): 396-402.
18. Gelinas P, Mckinnon CM. Effect of wheat variety, farming site, and bread-baking on total phenolics. Int J Food Sci Technol, 2006; 41(3): 329-332.

19. Kumar NS, Mukherjee PK, Bhadra S, Saha BP, Pal BC. Acetylcholinesterase inhibitory potential of a carbazole alkaloid, mahanimbine, from *Murraya koenigii*. Phytother Res, 2010; 24(4): 629-631.
20. Dineshkumar B, Mitra A, Mahadevappa M. Antidiabetic and hypolipidemic effects of mahanimbine (carbazole alkaloid) from *Murraya koenigii* (rutaceae) leaves. Int J Phytomed, 2010: 2(1): 22-30.
21. Ramsewak RS, Nair MG, Strasburg GM, DeWitt DL, Nitiss JL. Biologically active carbazole alkaloids from *Murraya koenigii*. J Agric Food Chem, 1999; 47(2): 444-447.
22. Jagtap S, Khare P, Mangal P, Kondepudi KK, Bishnoi M, Bhutani KK. Effect of mahanimbine, an alkaloid from curry leaves, on high-fat diet-induced adiposity, insulin resistance, and inflammatory alterations. BioFactors, 2017; 43(2): 220–231.
23. Srinivasan K. Black pepper and its pungent principle-piperine: A review of diverse physiological effects. Crit Rev Food Sci Nutr, 2007; 47(8): 735-48.
24. Shoba G, Joy D, Joseph T, Majeed M, Rajendran R, Srinivas PS. Influence of piperine on the pharmacokinetics of curcumin in animals and human volunteers. Planta Med, 1998; 64(4): 353-356.
25. Khajuria A, Thusu N, Zutshi U. Piperine modulates permeability characteristics of intestine by inducing alterations in membrane dynamics: Influence on brush border membrane fluidity, ultrastructure and enzyme kinetics. Phytomed, 2002; 9(3): 224-231.
26. Williams RJ, Spencer JP, Rice-Evans C. Flavonoids: antioxidants or signalling molecules? Free Radic Biol Med, 2004; 36(7): 838-849.
27. Russo GL, Russo M, Spagnuolo C, Tedesco I, Bilotto S, Iannitti R, et al. Quercetin: a pleiotropic kinase inhibitor against cancer. Cancer Treat Res, 2014; 159: 185-205.
28. Miles SL, McFarland M, Niles RM. Molecular and physiological actions of quercetin: need for clinical trials to assess its benefits in human disease. Nutr Rev, 2014; 72(11): 720-734.
29. D'Andrea G. Quercetin: A flavonol with multifaceted therapeutic applications? Fitoterapia, 2015; 106: 256-271.