Antimicrobial efficacy of fermented mango leaves beverage towards selected foodborne pathogens

Soo Peng Koh^{1*}, Shaiful Adzni Sharifudin¹, Rosmawati Abdullah¹, Nur Syazwani Abdul Hamid¹, Razali Mirad² and Razali Mustaffa³

¹Food Science and Technology Research Center, Malaysian Agricultural Research and Development Institute (MARDI) Headquarters, Persiaran MARDI-UPM, 43400 Selangor, Malaysia.

²Agrobiodiversity and Environmental Research Centre, Malaysian Agricultural Research and Development Institute (MARDI) Headquarters, Persiaran MARDI-UPM, 43400 Selangor, Malaysia.

³Horticulture Research Center, Malaysian Agricultural Research and Development Institute (MARDI) Headquarters, Persiaran MARDI-UPM, 43400 Selangor, Malaysia.
Email: karenkoh@mardi.gov.my

ABSTRACT

Aims: Fermented mango leaves of Chokanan variety was produced using selected symbiotic culture of bacteria and yeast (SCOBY) from MARDI's Collection of Functional Food Cultures (CFFC). The aim of this work was to investigate its functional benefits as food remedy to reduce the risk of food poisoning illness incidence.

Methodology and results: Five species of foodborne pathogens: *Escherichia coli* O157:H7 UPMEC32 (local isolate), *Salmonella typhimurium* ATCC®53648™, *Salmonella enteritidis* MDC15 (local isolate), *Listeria monocytogenes* ATCC®51772™ and *Streptococcus gallolyticus* (ATCC®9809™) were selected to examine the antimicrobial effect of fermented mango leaves beverage by means of agar well diffusion assay and broth microdilution method to determine its minimum bactericidal concentration (MBC_{>99}). In comparison with chemical inhibitor (acetic acid, 1%) and antibiotic (Penicillin streptomycin, 1%), the agar diffusion assay results confirmed the inhibition efficacy of fermented mango leaves beverage against all five foodborne pathogens tested. Particularly, fermented mango leaves beverage was showing a significant inhibitory effect ($P < 0.05$) against *S. gallolyticus*, whereas both acetic acid and penicillin streptomycin have no inhibitory activities at all towards this pathogen. Another antimicrobial activity assay using broth microdilution method also confirmed the 100% inhibition effect of fermented mango leaves beverage against these selected pathogenic microorganisms. Furthermore, the efficacy retained 100% inhibitory activities even though the fermented mango leaves beverage has been diluted to 50%. Synergetic effect of significant amount of multiple organic acids present in fermented mango leaves beverage were the main factors contributing to its potent antimicrobial properties and improvement taste after fermentation. On the contrary, little or no antimicrobial inhibitory activity was observed in all non-fermented mango leaves beverages treated samples.

Conclusion, significance and impact of study: This finding indicates that the potential of fermented mango leaves beverages as prophylaxis measures to reduce the risk of food poisoning incidence as it has shown a good antimicrobial effect against selected foodborne pathogens. Moreover, this fermented mango leaves beverage are more tasteful after gone through the microbial fermentation process. It is recommended to consume daily to reduce the incidence of food poisoning illness.

Keywords: Mango leaves, foodborne pathogens, antimicrobial activity, broth microdilution, fermentation

INTRODUCTION

Mango (*Mangifera indica* L.), is one of the popular horticulture fruits, belong to the *Anacardiaceae* family. This large evergreen tree is found in most tropical countries. Mango leaves possess some of the important metabolite compounds such as flavonoids, tannins, alkaloid and various polyphenolic substances (Shah *et al.*, 2010). It is well known for its multiple pharmacological effects including antidiabetic, anti-inflammatory,

anticancer, analgesic, antimicrobial and antioxidant activities (Islam *et al.*, 2010; Morsi *et al.*, 2010; Shah *et al.*, 2010; Ganogpichayagrai *et al.*, 2017). Mango fruit is rich with various polyphenolic compounds that can be detected in all parts of fruits. Particularly mangiferin, a xanthone derivative that is referred as a super antioxidant that contributing to its various pharmacological properties which is found abundantly in mango leaves (Shah *et al.*, 2010; Fernández-Ponce *et al.*, 2013).

There is an increasing threat of potent pathogenic foodborne microorganism, including antibiotic resistance. These microorganisms are more tolerant to various food processing method and preservation techniques. This phenomenon has caused frequent outbreak of food poisoning incidence and gained major concern of consumers and food industries (Tajkarimi *et al.*, 2010). Recent lifestyle also revealed that most of the people prefer eating outside and they are exposed to high risk of health problem if the food is prepared under poor hygiene condition. Typical symptoms of food poisoning illness include vomiting, abdominal cramps, diarrhea, nausea, headaches etc. may not be a life-threatening risk to healthy person. However, this kind of foodborne disease can cause severe illness to those pregnant women, children, elderly group or immunocompromised people (McCabe-Sellers and Beattie, 2004; Addis and Sisay, 2015). Therefore, there is an urgent attempt to look for natural products from plants that possess antimicrobial activities that are capable to inhibit the growth of pathogenic microorganism from plant sources to reduce the risk of foodborne illness incidence.

Plants are the safest and cheapest sources for antimicrobial agent (Gyawali and Ibrahim, 2014). Many plants had been used traditionally since long time without any adverse effects. Mango (*M. indica* L.) leaves is an important herb and commonly used in Ayurvedic and indigenous medical system. Bharti's study (2013) has reported that the presence of phytonutrients in the mango leaves extract plays a significant role on inhibiting various pathogenic organisms (*Salmonella typhi*, *Klebsiella pneumoniae*, *Enterobacter aerogens*, *Mycobacterium tuberculosis*, *Streptococcus pyrogens*, *Pseudomonas aeruginosa*, *Proteus vulgaris*, *Escherichia coli* and *Staphylococcus aureus*). However, the taste of mango leaves juice was awful, and people will only consume it when they are really sick. Therefore, the present study was focused on the antimicrobial efficacy of fermented mango leaves beverage towards selected foodborne pathogenic microorganisms.

MATERIALS AND METHODS

Preparation of dried mango leaves

Fresh mature green mango (*M. indica* L.) leaves, Chokanan variety were collected in MARDI Serdang Station (Selangor, Malaysia). The leaves were washed with water and dried in hot air oven at 50 °C with the moisture content of 5-6%. The dried leaves were pulverized and packed in aluminum foil and then kept at chiller at 4 °C prior to fermentation process.

Preparation of fermented beverage samples from dried mango leaves

A mixture of mango leaves powder with sugar at a ratio of 1:4 was prepared as non-fermented mango leaves beverage. Another set of fermented mango leaves beverage was prepared with the same concentration of

mango leaves suspension and were inoculated with 10% of the defined mixed culture of yeast (*Dekkera* sp.) and acetic acid bacteria (*Komagataibacter* sp.) from MARDI's Collection of Functional Food Cultures (CFFC) with the colony count of at least 1×10^8 CFU/mL. The culture was then incubated at 30 °C for 10 days. The pH and Brix value of both fermented and non-fermented mango leaves beverage samples were measured at the interval of 2 days using pH meter and refractometer, respectively.

Determination of organic acids content

Analyses of organic acids profile of fermented and non-fermented mango leaves phytonutrients were carried out with a high-performance liquid chromatography (HPLC), Alliance Separation Module (Waters, 2695), equip with a diode array detector (Waters, 2996). A 10 µL aliquot of sample solution was separated using Synergi 4 µm, Hydro-RP80A (250 × 4.6 mm) with the temperature controlled at 30 °C. The mobile phase consists of mobile phase A (20 mM KH_2PO_4 with adjusted pH 2.9) and mobile phase B (water) with a flow rate of 0.6 mL/min. Gradient elution was performed as follows: from 0 to 30 min, 100% A; from 30 to 45 min, linear gradients from 100 to 0% A; from 45 to 55 min, linear gradient from 0 to 100% A. Peak identification was made by comparing retention times and UV spectra at 190, 210 and 254 nm with authentic organic acids compounds. Quantification was made using calibration curves obtained by injecting known amounts of pure organic acids as external standard. All analyses were performed in triplicate.

Pathogenic strains and culture condition

In the present study, five types of foodborne pathogens: *E. coli* O157: H7 UPMEC32 (local isolate), *S. typhimurium* ATCC®53648™, *S. enteritidis* MDC15 (local isolate), *L. monocytogenes* ATCC®51772™ and *S. gallolyticus* (ATCC®9809™) were selected to determine the minimum bactericidal concentration ($\text{MBC}_{>99}$) of fermented mango leaves beverages. All ATCC cultures were purchased from American Type Culture Collection (ATCC, Rockville, MD). All bacterial cultures were revived from glycerol stock and streak onto selective agar media as prepared according to manufacturer's protocol and incubated overnight at 37 °C for 24 h.

Antimicrobial activity assay

Agar well diffusion assay

The Mueller Hinton agar plate containing 10^8 CFU/mL of selected pathogen strain was prepared. A sterile pipet tip was used to make wells with a diameter of 6 mm. Approximately 20 µL of Mueller Hinton broth was added to each well in order to seal it to avoid leakage. Then, 100 µL samples (fermented and non-fermented mango leaves) was added into the wells and allowed it to diffuse onto agar for the first 90 min at room temperature,

followed by incubation at 37 °C for 24 h. The antimicrobial effect was recorded by calculating the diameter of inhibition clear zone that appeared. The chemical inhibitor (acetic acid, 1%) and antibiotic (penicillin streptomycin, 1%) were used as a comparison control.

Determination of minimum bactericidal concentration (MBC_{>99})

Escherichia coli O157: H7 UPMEC32 (local isolate), *S. typhimurium* ATCC®53648™, *S. enteritidis* MDC15 (local isolate), *L. monocytogenes* ATCC®51772™ and *S. gallolyticus* (ATCC®9809™) were cultured onto tryptone soy agar individually and incubated overnight. A loopful of foodborne pathogen culture from each tryptone soy agar was inoculated onto tryptone soy broth and then incubated at the temperature of 37 °C for 16 h at the agitation rate of 160 rpm to obtain the suspension culture with the initial colony count of 10⁹ CFU/mL. The MBC_{>99} for each microbe was determined using broth microdilution technique as described in Koh *et al.* (2017). Both non-fermented and fermented mango leaves beverage were used as an initial working concentration to determine its MBC_{>99}. Two wells served as control, consists of microbe culture without treatment and sterilized growth media. Each well contained 120 µL of the test material in serially descending concentration. An amount of 20 µL of inoculum containing about 1×10⁹ CFU/mL foodborne pathogen suspension was added onto each well and was rotated using microtiter plate shaker before incubated at the temperature of 37 °C for 24 h. After incubation, the serial dilutions were performed in the microcentrifuge tube using micropipette and the plate count for each dilution was analyzed in triplicate.

Statistical analysis

The experimental results were analyzed using SPSS software (SPSS statistics version 16). All data were expressed as the mean ± standard deviation of triplicate analysis. A one-way analysis of variance (ANOVA) at the 5% significance level was used to determine significant differences (P<0.05) between means.

RESULTS AND DISCUSSION

Characterization of fermented mango leaves beverage

In the past, mango leaves were used as traditional medicine in the treatment of diabetes to reduce the illness side effects and secondary complications as it is a natural source with total flavonoids and phenolic contents (Morsi *et al.*, 2010). Even though the mango leaves reported to have multiple pharmacological effects, its bitter astringent taste is a drawback. Therefore, one of the objectives of this work was to transform this mango leaves into a palatable fermented mango leave beverage using a symbiotic culture of acetic acid bacteria and yeast

(SCOBY). This specific SCOBY strain consortium was selected as it was believed to be able to produce mango beverage with no astringent taste. The product was designed to have a closer taste to Kombucha sugar tea product which is produced using a pool mixture of yeast and acetic acid bacteria and is consumed worldwide for its refreshing and beneficial properties on human health (Jayabalan *et al.*, 2014).

In our study, we have selected two pure cultures of SCOBY strains (*Dekkera* sp. and *Komagataibacter* sp.) to transform mango leaves into new functional beverage. Generally, the pH and brix value of the fermented mango leaves were found to reduce significantly (P<0.05) throughout 10 days of fermentation. This indicates that SCOBY strains were nutritionally supported and able to grow well in the mango leaves media (Table 1). During the fermentation of sugared mango leaves infusion, disaccharides were decomposed and converted into simple sugar by the influence of microbial enzymes. This provides nutrition to support the microbial growth. Consumption of soluble solid compounds by SCOBY strain has caused a reduction in Brix value. Furthermore, organic acids profile analysis on fermented mango leaves elucidated that the drastic drop in pH was due to the significant amount of various organic acids produced (P<0.05) after fermentation, particularly acetic acid which was present abundantly. The remarkable increment of acetic acid in fermented mango leaves beverage was produced by acetic acid bacteria indicating that this SCOBY strains can adapt and grow well in mango leave media only. Acetic acid, a volatile organic acid is the major component responsible for a pungent flavor and taste. The presence of various organic acids produced by SCOBY strains have contributed to its palatable taste of fermented mango leaves beverage. Bio-based acetic acid was reported to have multiple health benefits. For example, the presence of acetic acid in vinegar was reported to exhibit various pharmacological effect such as anti-glycemic effect (Johnston and Gaas, 2006); anti-hypertensive effects (Kondo *et al.*, 2001), anti-tumor activity (Mimura *et al.*, 2004; Nanda *et al.*, 2004) etc. In the past, acetic acid is a topical active ingredient used to treat pseudomonal wound infection (Nagoba *et al.*, 2013).

Other types of organic acids including citric acid, oxalic acid, malic acid, kojic acid and quinic acid also exhibited an increment trend with fermentation days as shown in Table 1. However, the concentration of these organic acids was found to decrease slightly after reaching optimum production at day 8. Past findings of these organic acids have revealed their numerous functional benefits. Citric acid is an important organic acid found in fermented mango leaves beverage after the SCOBY fermentation process. Citric acid provides a pleasant sour taste which may influence our appetite and enhance the flavor. It is the most versatile organic acid used in food, cosmetics and pharmaceutical field due to its high solubility in water. Combination of citric acid and malic acid were reported to have an important role in the therapy of ischemic heart disease (Tang *et al.*, 2013).

Table 1: Change of pH and Brix value and organic acids content of mango leaves beverage at the interval time of 10 days fermentation.

Day	pH value	Brix value	Acetic acid	Citric acid	Oxalic acid	Malic acid	Kojic acid	Quinic acid
			(ug/mL)					
0	5.05±0.00 ^f	10.22±0.04 ^f	0.00±0.00 ^a	0.00±0.00 ^a	18.46±0.93 ^a	23.35±3.00 ^a	0.612±0.09 ^a	345.67±12.12 ^a
2	2.85±0.02 ^e	9.08±0.10 ^e	4300.80±96.46 ^b	40.56±7.74 ^b	19.00±0.32 ^a	26.47±1.49 ^a	1.70±0.22 ^b	382.39±8.83 ^b
4	2.65±0.01 ^d	8.78±0.04 ^d	9063.25±134.73 ^c	75.33±7.68 ^c	21.95±1.39 ^b	44.77±6.38 ^b	2.78±0.12 ^c	374.08±8.73 ^b
6	2.79±0.00 ^c	8.18±0.08 ^c	13574.09±141.89 ^d	84.35±6.62 ^{c,d}	26.13±0.97 ^{c,d}	59.87±13.65 ^c	3.31±0.27 ^d	417.63±10.94 ^c
8	2.76±0.01 ^b	7.82±0.04 ^b	16565.80±1493.6 ^e	109.12±8.00 ^e	24.93±0.99 ^c	66.21±5.61 ^c	3.30±0.24 ^d	524.29±8.84 ^e
10	2.74±0.01 ^a	7.68±0.04 ^a	14574.80±1323.6 ^d	99.48±12.62 ^{d,e}	22.76±3.12 ^{b,c}	43.42±9.52 ^b	2.866±0.52 ^c	474.31±4.70 ^d

^aEach value in the Table represents the mean ± standard deviation from triplicate analyses. Mean values with different superscripts in the same column are significantly different at P<0.05.

Table 2: Well diffusion assay of fermented mango leaves beverage against selected pathogenic microorganisms^a.

Pathogens	Inhibition zone (mm) ± Standard deviation		
	Fermented ML	Acetic acid (1%)	Penicillin Streptomycin (1%)
<i>S. typhimurium</i>	18.00±0.00 ^b	10.67±0.71 ^a	18.33±1.32 ^b
<i>E. coli</i> 0157:H7	18.00±0.00 ^b	12.67±1.94 ^a	17.67±0.50 ^b
<i>S. enteritidis</i>	15.00±0.00 ^b	10.78±0.44 ^a	19.44±0.73 ^c
<i>S. gallolyticus</i>	18.00±0.00 ^a	Not Detected	Not Detected
<i>L. monocytogenes</i>	15.00±0.00 ^a	Not Detected	20.11±0.33 ^b

^aEach value in the Table represents the mean±standard deviation from triplicate analyses. Mean values with different superscripts in the same row are significantly different at P<0.05.

Oxalic acid occurs naturally in high levels in many common foods, including potatoes, beets, broccoli, carrot, fruits, nuts, legumes, grains etc. Oxalic acid is known as an anti-nutrient compound as it can combine with calcium and some other minerals to create oxalate crystals, which can contribute to kidney stones, gout etc. when presents in high amount in our body. However, low concentration of oxalic acid is essential to maintain peristaltic motion in our body. Therefore, the presence of small amount of oxalic acid (<30 µg/mL) in fermented mango leaves beverage may help to maintain the lower part of ileum. Quinic acid was reported to support the synthesis of tryptophan and nicotinamide in the gastrointestinal (GI) tract, thus nutritionally providing essential metabolic ingredients to humans (Pero *et al.*, 2009). Kojic acid, a skin brightening agent, used for protecting the radiant skin by neutralizing free radicals present in the environment. It is one of the natural by-products of fermented malting rice produced during Japanese wine sake production (Cheche, 2016).

Inhibitory effect of fermented mango leaves towards selected foodborne pathogenic microorganisms

A total of five foodborne pathogenic microorganisms have been selected to examine the inhibitory activities of fermented mango leaves beverage, which were *E. coli* O157:H7 UPMEC32 (local isolate), *S. typhimurium* ATCC®53648TM, *S. enteritidis* MDC15 (local isolate), *L. monocytogenes* ATCC®51772TM and *S. gallolyticus*

(ATCC®9809TM). By means of agar diffusion assay, fermented mango leaves showed a remarkable inhibitory effect against all five foodborne pathogens as summarized in Table 2. Particularly, fermented mango leaves beverage revealed to have strong significant inhibitory effect (P<0.05) against *S. gallolyticus*. On the contrary, both chemical inhibitors (acetic acid, 1% and penicillin streptomycin, 1%) showed no inhibitory activities at all towards *S. gallolyticus* as confirmed in agar diffusion assay.

To further investigate the capability of this antimicrobial effect, another antimicrobial activity assay using broth microdilution method was conducted to determine its minimum bactericidal concentration (MBC_{>99}). Overall, fermented mango leaves beverage revealed 100% inhibition effect against these selected pathogenic microorganisms (Figure 1). More interestingly, the antimicrobial efficacy retained 100% inhibitory activities although it has been diluted to 50% with the intention to mimic stomach condition with the presence of foods. These findings demonstrated the strong inhibitory effect against these selected foodborne pathogenic microorganisms. On the contrary, little or no antimicrobial inhibitory activity was observed in all non-fermented mango leaves beverages treated samples. Significant increment of multiple organic acids presents in fermented mango leaves beverage after gone through controlled bio-fermentation process using SCOBY strains were the main contributing factors for its potent antimicrobial inhibitory activities.

Figure 1: Minimum bactericidal concentration (MBC₉₉) of non-fermented and fermented mango leaves beverages against selected pathogenic microorganisms: a) *E. coli* 0157:H7; b) *L. monocytogenes*; c) *S. enteritidis*; d) *S. typhimurium*; e) *S. gallolyticus*.

Many findings have reported the antimicrobial activity of acetic acid, citric acid, kojic acid, malic acid and quinic acid against various types of pathogenic microorganisms (Raybaudi-Massilia *et al.*, 2009; In *et al.*, 2013; Halstead *et al.*, 2015; Nurunnabi *et al.*, 2018; Bai *et al.*, 2018). Acetic acid showed good antibacterial activity on localized infections and burn wound sepsis, which are key concerns in the treatment of burns patients (Halstead *et al.*, 2015). Quinic acid, another natural organic acid was shown to exhibit potent antibacterial activity against *Staphylococcus aureus* by reducing succinate dehydrogenase activity (Bai *et al.*, 2018). Studies of the cellular functions demonstrated that quinic acid could significantly decrease the intracellular pH and ATP

concentration, consequently, cause a remarkably effect to reduce the DNA content of *S. aureus* and interact with genomic DNA directly. Raybaudi-Massilia *et al.* (2009) had reported a potent inhibitory effect of malic acid against *L. monocytogenes*, *S. enteritidis* and *E. coli* O157:H7 in apple, pear and melon juices. On the other hand, kojic acid, produced by *Aspergillus luteo-virescens* was found to have strong antagonistic against both Gram-positive and Gram-negative bacteria (Morton *et al.*, 1945). Synergetic effect of these multiple organic acids has confirmed and supported the potent antimicrobial effect of fermented mango leave beverage against selected foodborne pathogenic microorganisms. Furthermore, the fermented mango leaves beverage was more palatable

because of the presence of various organic acids produced by these beneficial microorganisms during fermentation process. This phenomenon demonstrated the potential of fermented mango leaves beverage to be marketed as functional beverage to maintain good health.

CONCLUSION

The SCOBY fermentation has transformed mango leaves into functional beverage by producing significant amount of bio-based organic acids. In this study, the synergetic effect of various organic acids that has contributed to potent antimicrobial effect against pathogenic microorganisms is confirmed via both agar diffusion and broth microdilution assay. The efficacy of the fermented mango leaves beverage to inhibit various foodborne pathogens is expected to reduce the risk of food poisoning illness incidence and maintain good quality of life with the presence of various beneficial metabolites from mango leaves.

ACKNOWLEDGEMENT

This study was supported by Horticulture Research Centre, Malaysian Agricultural Research and Development Institute (MARDI) and financially funded by Government Development Fund RMK-11 (P21003004050001).

REFERENCES

- Addis, M. and Sisay, D. (2015). A review on major food borne bacterial illness. *Journal of Tropical Diseases* 3(4), 1-7.
- Bai, J., Wu, Y., Zhong, K., Xiao, K., Liu, L., Huang, Y., Wang, Z. and Gao, H. (2018). A comparative study on the effects of quinic acid and shikimic acid on cellular functions of *Staphylococcus aureus*. *Journal of Food Protection* 81(7), 1187-1192.
- Bharti, R. P. (2013). Studies on antimicrobial activity and phytochemical profile of *Mangifera indica* leaf extract. *Journal of Environmental Science, Toxicology and Food Technology* 7(3), 74-78.
- Cheche, V. (2016). Kojiesan skin lightener uses natural byproduct of Japanese rice wine. <http://lifestyle.inquirer.net/232402/kojiesan-skin-lightener-uses-natural-byproduct-of-japanese-rice-wine>. [Retrieved on 8 July 2016]
- Fernández-Ponce, M. T., Casas, L., Mantell, C. and Martínez de la Ossa, E. J. (2013). Potential use of mango leaves extracts obtained by high pressure technologies in cosmetic, pharmaceuticals and food industries. *Chemical Engineering Transactions* 23, 1147-1152.
- Ganogpichayagrai, A., Palanuvej, C. and Ruangrungsi, N. (2017). Antidiabetic and anticancer activities of *Mangifera indica* cv. Okrong leaves. *Journal of Advanced Pharmaceutical Technology and Research* 8(1), 19-24.
- Gyawali, R. and Ibrahim, S. A. (2014). Natural products as antimicrobial agents. *Food Control* 46, 412-429.
- Halstead, F. D., Rauf, M., Moiemmen, N. S., Bamford, A., Wearn, C. M., Fraise, A. P., Lund, P. A., Oppenheim, B. A., Mark, A. and Webber, M. A. (2015). The antibacterial activity of acetic acid against biofilm-producing pathogens of relevance to burns patients. *PLoS One* 10(9), e0136190.
- In, Y. W., Kim, J. J., Kim, H. J. and Oh, S. W. (2013). Antimicrobial activities of acetic acid, citric acid and lactic acid against *Shigella* species. *Journal of Food Safety* 33, 79-85.
- Islam, M. R., Mannan, M. A., Kabir, M. H. B., Islam, A. and Olival, K. J. (2010). Analgesic, anti-inflammatory and antimicrobial effects of ethanol extracts of mango leaves. *Journal of the Bangladesh Agricultural University* 8(2), 239-244.
- Jayabalan, R., Malbaša, R. V., Lončar, E. S., Vitas, J. S. and Sathishkumar, M. (2014). A review on Kombucha tea - Microbiology, composition, fermentation, beneficial effects, toxicity and tea fungus. *Comprehensive Reviews in Food Science and Food Safety* 13, 538-550.
- Johnston, C. S. and Gaas, C. A. (2006). Vinegar: Medicinal uses and antiglycemic effect. *MedGenMed* 8(2), 61.
- Koh, S. P., Aziz, N., Sharifudin, S. A., Abdullah R., Hamid, N. S. A. and Sarip, J. (2017). Potential of fermented papaya beverage in the prevention of foodborne illness incidence. *Food Research* 1(4), 109-113.
- Kondo, S., Tayama, K., Tsukamoto, Y., Ikeda K. and Yamori, Y. (2001). Antihypertensive effects of acetic acid and vinegar on spontaneously hypertensive rats. *Bioscience, Biotechnology and Biochemistry* 65, 2690-2694.
- Mccabe-Sellers, B. J. and Beattie, S. E. (2004). Food Safety: Emerging trends in foodborne illness surveillance and prevention. *Journal of the American Dietetic Association* 104, 1708-1717.
- Mimura, A., Suzuki, Y., Toshima, Y., Yazaki, S., Ohtsuki, T., Ui, S. and Hyodoh, F. (2004). Induction of apoptosis in human leukemia cells by naturally fermented sugar cane vinegar (kibizu) of Amami Ohshima Island. *Biofactors* 22, 93-97.
- Morsi, R. M. Y., EL-Tahan, N. R. and El-Hadad, A. M. A. (2010). Effect of aqueous extract *Mangifera indica* leaves as functional foods. *Journal of Applied Sciences Research* 6(6), 712-721.
- Morton, H. E., Kocholaty, W., Junowiczkocholaty, R. and Kelner, A. (1945). Toxicity and antibiotic activity of kojic acid produced by *Aspergillus luteo-virescens*. *Journal of Bacteriology* 50(5), 579-584.
- Nagoba, B. S., Selkar, S. P., Wadher, K. J. and Gandhi, R. C. (2013). Acetic acid treatment of psedomonal wound infections - A reviews. *Journal of Infection and Public Health* 6, 410-415.
- Nanda, K., Miyoshi, N., Nakamura, Y., Shimoji, Y., Tamura, Y., Nishikawa, Y., Uenakai, K., Kohno, H. and Tanaka, T. (2004). Extract of vinegar "Kurosu"

from unpolished rice inhibits the proliferation of human cancer cells. *Journal of Experimental and Clinical Cancer Research* **23**(1), 69-75.

Nurunnabi, T. R., Al-Majmaie, S., Nakouti, I., Nahar, L., Mahbubur Rahman, S. M., Sohrab, M. H., Billah, M. M., Ismail, F. M. D., Sharples, G. P., Satyajit, D. and Sarker, S. D. (2018). Antimicrobial activity of kojic acid from endophytic fungus *Colletotrichum gloeosporioides* isolated from *Sonneratia apetala*, a mangrove plant of the Sundarbans. *Asian Pacific Journal of Tropical Medicine* **11**(5), 350-354.

Pero, R. W., Lund, H. and Leanderson, T. (2009). Antioxidant metabolism induced by quinic acid. Increased urinary excretion of tryptophan and nicotinamide. *Phytotherapy Research* **23**(3), 335-346.

Raybaudi-Massilia, R. M., Mosqueda-Melgar, J. and Martín-Belloso, O. (2009). Antimicrobial activity of malic acid against *Listeria monocytogenes*, *Salmonella Enteritidis* and *Escherichia coli* O157:H7 in apple, pear and melon juices. *Food Control* **20**(2), 105-112.

Shah, K. A., Patel, M. B., Patel, R. J. and Parmer, P. K. (2010). *Mangifera Indica* (Mango). *Pharmacognosy Review* **4**(7), 42-48.

Tajkarimi, M. Ibrahim, S. and Cliver, D. (2010). Antimicrobial herb and spice compounds in food. *Food Control* **21**(9), 1199-1218.

Tang, X., Liu, J., Li, P., Li, L., Lin, C., Zheng, Y., Hou, J. and Li, D. (2013). The cardioprotective effects of citric acid and L-malic acid on myocardial ischemia/reperfusion injury. *Evidence-based Complementary and Alternative Medicine* **2013**(820695), 1-11.