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MINI REVIEW

Synbiotic and antioxidant activity of fruit by-products and their effect on human health

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Abstract

Food supplements are extensively used as a natural remedy to improve human health condition. Considerable progress has been reported recently by several studies to analyse the bioactive substances and their functional activities of fruit by-product. The food industry generates a vast amount of wastes during manufacturing or processing, which are mainly skins, kernels, and seeds. These by-products contain valuable bioactive compounds such as antioxidants, vitamins, minerals, and indigestible food ingredients called prebiotics. Peels from fruits like yellow rambutan, green kiwi, mango, and papaya exhibit a strong anti-proliferative, anti-cardiovascular, anti-oxidant, and hepatoprotective effects due to the presence of bioactive compounds namely flavonoid, B-type catechin dimer, and penta-O-galloyl-glucoside. This review will illustrate a new concept of functional foods by providing information on alternative sources of bioactive compounds from food by-product and their efficacy in human nutrition. This study will also recapitulate the presence of bioactive components in fruit by-product, their way of action, constitution, health benefits, and probable therapeutic action in the treatment of disease prevention.

1. Introduction

The most commonly used horticultural crops are fruits and vegetables among other goods which can consume as fresh, processed, or minimally processed form because of their nutritious components. Due to the changing pattern of diet and increasing population, consumer demand for fruits and vegetables has increased drastically (Sagar *et al*., 2018). However, Irfanoglu *et al*. (2014), have reckoned that around one-third of the human food is wasted or lost worldwide, which is near to 1.3 billion tons of food each year. Actually, losses and wastage are high (reaching up to 60%) in fruit and vegetable processing, which become a critical issue for human nutrition and habitat (Sagar *et al*., 2018). Only a small quantity of these is utilised as fertiliser and pet food (Hernández-Alcántara *et al*., 2016). Moreover, these by-product losses are not only the losses of food products, but also represent the losses of other assets, i.e., energy, field, water, compost chemicals, and manpower (Sagar *et al*., 2018).

Studies have reported that the skin part of grapes and bananas; and seeds of mangoes and jackfruits comprise of high phenolic concentrations, which is 15% higher than the amount in fruit pulp (Sagar *et al*., 2018). Phytochemical information provides the basis for developing new functional beverages and foods (Ibrahim *et al*., 2017). Fruits waste can be used to extract and isolate potential prebiotics and probiotics that can be the cheapest source for food, textile, and pharmaceutical industries. Therefore, the appropriate utilisation of waste materials attained from the food industry can be a new initiative towards sustainable development to alleviate environmental pollution and to improve health by adding the health-improving elements such as dietary fibres, phenols, vitamins, carotenoids, and others (Sagar *et al*., 2018). According to the study of Wadhwa (2016), fruit by-product is rich in antioxidants and other bioactive compounds that protect human health from several degenerative diseases. It is reported that the phenolic compounds and other antioxidants in fruit by-product exhibit anti-microbial, anti-cancer and anti-oxidative effects; reduce the risk of cardiovascular diseases, capillary fragility, plasma cholesterol level, and inhibit platelet aggregation (Wadhwa, 2016). Yellow rambutan (*Nephelium lappaceum*) peel extract exhibits a strong

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anti-proliferative activity in osteosarcoma and breast cancer cells and also reduces the proliferation of colon tumour cells because of the presence of the flavonoid compound (Khaizill *et al*., 2013). Green kiwi peels can be utilised as a source of natural functionalizing ingredients with several health benefits that contain higher phenolic content particularly B-type catechin dimer and showed cytotoxicity and anti-inflammatory activity (Dias *et al*., 2020). Studies have indicated that mango peel and seed kernel extract contain penta-O-galloyl-glucoside, which exhibits several bioactivities including anti-cardiovascular, anti-oxidant, anti-tumour, and hepatoprotective effects (Wadhwa, 2016). This review aims to briefly discuss the availability of bioactive compounds in fruit by-product, their mechanisms of action, and the current insights into their therapeutic potential for preventing chronic diseases. Although several studies have shown the beneficial effects of such compounds on human health, further research should be conducted on the acquisition of new strains to produce synbiotics, clinical trials, and safety of use to achieve accurate evidence.

2. The extent of fruit by-product

The unconsumed parts of fruit and vegetables are known as by-products which are simply discarded for multiple reasons, i.e., inadequate handling operations and morphological characteristics of the product. However, the quantity of fruit waste changes based on product and morphological materials, including peels, pulp, seeds, kernel, pomace, and roots (Sagar *et al*., 2018). With respect to the literature review, apples can produce 10.91% by-product from seeds and 89.9% pulp as an end product during cutting. Papaya generates around 8.5%, 6.5%, 32% and 53% of peel residue, seeds, the pulp (not usable), and finished product during dicing, respectively. During peeling, mandarins yield 16% of peels and 84% of the final product. The processing of pineapple generates approximately 14%, 9%, 15%, 15% and 48% of peels, core, pulp, top and finished product, respectively. Mango processing yields around 11% of peels, 13.5% of seeds, 18% of the core, and 58% of the final product (Joshi *et al*., 2012; Sagar *et al*., 2018). Furthermore, fruits and vegetables yield about 5.5 million metric tons (MMT) of by-product including pomace. During processing grape and wine, the industry can produce approximately 5 - 9 MMT of solid waste per year globally, in which 20% - 30% are processed materials. Canning and frozen processing yields around 6 MMT of residue from fruits and vegetables yearly, which consist of 20% - 30% leaves, petioles, and stems of broccoli or carrot (Sagar *et al*., 2018).

3. Major bioactive component sources

Biologically active compounds and phenolic components are present in peels, seeds, and pomace of fruits. Mostly, apples, pears, banana, dragon fruit, berries, and mangoes are considerably higher than those found in their edible parts (Wadhwa, 2016). This finding suggested that these wastes have the potential for isolating bioactive compounds. Table 1 represents the applications of food by-product as sustainable ingredients. Studies have shown that the pomace of orange, raspberry, pear, watermelon, peach, banana, apple, cherry, durian seeds, date pits and mango peels are used as functional ingredients in processed food because of their pectin carotenoids and bound antioxidant contents (Wadhwa, 2016). According to Hernández-Alcántara *et al*. (2016), fruit (e.g., banana, apple) peels and carrot pulp residue have been found to be good sources of fibre and antioxidants which functioning as prebiotics for the growth of lactic acid bacteria. Table 2 shows the amount of edible part and the by-product of different fruits produced during processing in the food industry (Goni and Hervert-Hernandez, 2012; Barbulova *et al*., 2015). Pineapple by-product can be utilised as alternative cheapest source for probiotic cultivation in comparison to expensive MRS (De Man, Rogosa and Sharpe agar) medium. Moreover, after fermentation, these waste recoveries can develop the overall economic processing unit in a country (Pyar *et al*., 2014).

3.1 Watermelon peel

Malaysia's watermelon production in 2017 was 172,275.36 metric tons (Department of Agriculture of Malaysia, 2017). Watermelon has potential therapeutic effects, which can be attributed to its antioxidant activity (Koocheki *et al*., 2007). Particularly, the antioxidant properties of citrulline in watermelon rind helps to protect humans from free radical damage. Moreover, citrulline can be converted into a type of amino acid known as arginine, which plays a significant role in the immune and circulatory systems and the human heart (Rimando and Perkins-Veazie, 2005). Watermelon rind is believed to have the ability to relax blood vessels, and work for cancer, cardiovascular diseases, apart from addressing erectile function (Ibrahim *et al*., 2017). Recent studies have found that watermelon rind powder has been used to prepare cake batter for bakery products by mixing with flour (Al-Sayed and Ahmed, 2013).

3.2 Grape peels and seeds

According to Food and Agriculture Organization (FAO) (2010), the world total grape production is 67116255 tons, and China is the top grape-producing (8651831 tons) country all over the world (Ministry of

Table 1. Applications of food by-products as sustainable ingredients

Byproduct	Dose	Function	Bioactive compounds	References
Chestnut waste flour	2%	Promote health	Source of phenolic compound and probiotic	Ozcan *et al.* (2016)
Apple pulp residue	2.5 - 10%	Promote health	Source of fibre	Issar *et al. (*2016)
Peel of banana	1%	Promote health	Source of fiber and probiotic	do Espírito Santo *et al.* (2012)
Powder made by pineapple peel	1%	Promote health	Act as probiotic	Iriondo-Dehond *et al.* (2018)
Peel of Passion fruit	0.70%	Promote health	Rich source of fibre	do Espírito Santo *et al.* (2012)
Grape refuse flour	10, 20, and 50 g/L	Promote health	Source of phenolic compound and probiotic	Frumento *et al.* (2013)
Seed from pomegranate fruit	25 mg/L	Technological benefit	Source of antioxidant	Iriondo-Dehond *et al.* (2018)
Grape peel flour	0.167- 1 g/100 g	Promote health	Source of polyphenol	Karnopp *et al.* (2017)
Grapeseed	25 mg/L	Technological benefit	Source of antioxidant antimicrobial activities	Iriondo-Dehond *et al.* (2018)
Date waste	0.5, 1, and 2 ratios of dry powder/date syrup	Technological and health-promoting benefit	Source of phenolic compound	Jridi *et al.* (2015)
Almond skin	100 to 400 mg/L	Technological benefit	Source of antioxidant	Nadeem *et al.* (2014)
Pomegranate skin	100 ml/25 g	Technological benefit	Antioxidant and antimicrobial activities	Shan *et al.* (2011)

Table 2. Quantities of some fruit by-product produced in food processing industries

Sources	By-Products	Edible Part
Apple	Pulp, seed core (11%)	89%
Banana	Peel (above 30%)	70%
Mandarin	Peels (16%)	84%
Mango	Seeds, peels, unusable pulp (42%)	58%
Citrus fruits	Peel (66%)	44%
Papaya	Seeds, peels, unusable pulp (47%)	53%
Passion fruit	Rind, seeds (75%)	25%
Pineapple	Core, peels, upper part, pulp (52%)	48%
Jackfruit	Peel, Seeds (50% –70%)	30%–50%
Grapes	Peel, seeds, stalk (20%)	80%
Durian	Skin, seeds (60% -70%)	30 % – 40%
Dragon fruit	Skin, seeds (30% -45%)	55% -70%

Source: Goni and Hervert-Hernandez (2012); Barbulova *et al*. (2015); Sagar *et al*. (2018)

Commerce and Industry Government of India. 2011). Grape peels and seeds contain antioxidants especially phenolic components, for example, gallic acid, cyanidin-3-glucoside, epicatechin, catechin gallate, and resveratrol which contribute to reducing oxidative and free radical activities. Therefore, grape wastes can be an alternative natural source of bioactive components and can be used to develop new value-added functional food and pharmaceuticals drug.

3.3 Pineapple waste

In Malaysia, pineapple uses 6.3% agro-food area with an approximate production of 340,721.95 metric tons (Department of Agriculture of Malaysia, 2017). Pineapple by-product shows prebiotic characteristics which can be applied commercially in the formulations of new functional food (Sah *et al*., 2016). According to Pyar *et al*. (2014), pineapple waste is a possible source of carbon and other nutrition for the development of lactic acid by microbial systems. During canning operation, around 30% of pineapples waste is produced which can be responsible for the hostile environment if not used properly due to low protein content, high amount of carbohydrates, and fibres (Bhargava *et al.,* 2008; Nadzirah *et al.,* 2013; Pyar *et al.,* 2014). Therefore, these fruit by-product could be the cheapest alternative nutrition growth source for probiotics.

3.4 Banana Peel

The total production of banana in Malaysia was 350,492.59 metric tons in 2017 (Department of Agriculture of Malaysia, 2017). Research findings showed that peel and seed fractions of banana contain higher antioxidants and phenolic compounds than that of in their pulp (González-Montelongo *et al.,* 2010). The most common antioxidant components found in the banana peel are ascorbic acid, phenolic groups, tocopherol, dopamine, beta carotene, and gallocatechol

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(Bankar *et al.,* 2010). Moreover, as a rich source of antioxidant, banana considered the suitable candidate as a functional food as opposed to cancer and heart disease (Ibrahim *et al.,* 2017).

3.5 Papaya peel and seeds

Malaysia produced 83,796.99 metric tons papaya in 2017 (Department of Agriculture of Malaysia 2017). In papaya processing, the common by-products are papaya peel and seeds which represent around 8.5 to 12% of fruit weight. These by-products are the natural source of value-added nutrients and can be utilised as new nutraceutical foods, dietary additives, and pharmaceutical products (Pathak *et al.,* 2018). Papaya peel extracts can be used in probiotic production which represents functional effects on urogenital, digestive, and immune systems in human health and also shows a protective effect against inflammation and cardiovascular diseases (Hardia and Iqbal, 2014; Pathak *et al.*, 2018). In a quantitative analysis, 20.23mg/ml sugar concentration was found from papaya peel extract, and the growth of Lactobacillus in the extract was determined at optimum pH (7.0) and temperature (37°C) with a survival rate of 2.0% in NaCl (Hardia and Iqbal, 2014).

4. Antioxidants

Synthetic antioxidants are often used in the food industry for preservation purposes for a long time. Butylated hydroxyanizole (BHA) and butylated hydroxytoluene (BHT) are mostly used antioxidant additives for the preservation purpose and stabilizing the coldness, colour, aroma, and nutritive value of food products (Wadhwa, 2016). However, it is reported that BHT can be toxic if added at higher doses (Schilderman *et al.,* 1995). Hence, the demand for replacing synthetic antioxidants from alternative natural sources is increasing tremendously. Plant material is the popular source of antioxidants. Mainly antioxidants can be categorized into two groups concerning the mode of action (Grajek *et al.,* 2005). Firstly, the chemical substances of antioxidants can inhibit the amplification of free radical chain by donating hydrogen compound to radicals and stabilizing the radical electrons which are relocated. Tocopherols, hydrochinons, and gallusans exhibited this type of mode of action. Secondly, a synergistic way of action is demonstrated by another group of antioxidants, including oxygen scavengers and chelators which helps to bind ions that related to free radical formation. Moreover, their function involves distributing hydrogen to phenoxy radicals for regenerating antioxidant's primary function (Grajek *et al.,* 2005). The concentrations of phytochemicals and other phenolic compounds in different fruit peels, seeds/stones, and pomace (citrus fruits, apples, peaches, pears, banana, pomegranate, berries, and mangoes) found to be considerably greater than their respective edible portion. The result from these findings suggested that these fruit by-products could be the prospective natural sources for separating bioactive components (Wadhwa, 2016).

4.1 Mechanism of action of antioxidants

Epidemiological information and some clinical trials give sufficient evidence that antioxidants play a significant role in the preclusion of cancer and cardiovascular diseases (Grajek *et al.,* 2005). Antioxidants may act as scavengers for metal chelators and reactive oxygens to decrease oxidative damage and work as a safeguard for human cells. DNA damage is considered as the principal reason for the beginning of cancerogenic aggravated by mutagenic factors like free radicals which control the cell growth, separation, and combine the signal of extracellular and intracellular cell response (Diplock *et al.,* 1999). Based on the epidemiological study, it is revealed that higher antioxidant consumption may reduce the risk of cancer diseases impressively. The factors involved in inhibiting cancer development are as follows: β-carotene, resveratrol, curcumin, gallusan, epigallocatechine, and gingerol (Shklar, 1998). The progression of the remaining tumours is also remarkably suppressed by antioxidants. Nowadays, three principle mechanisms are considered to be responsible for the destruction and inhibition. Firstly, improving the immunological function that helps in proper identification and demolition of the cancer-causing cells in the organism. The killing factors involving tumours necrosis factor α (TNF-α) are produced by macrophages and β tumour necrosis factor β (TNF-β) generated by lymphocytes. Antioxidants namely α-tocopherol and β-carotene exhibited higher cytotoxic cells production which increases the cytokine production and assists in cancer cell migration leading to the destruction of a tumour's rapid growth. Secondly, mechanism of tumour destruction is associated with genetic characteristic where the antioxidants contribute in increasing p53 (wild type) gene expression whose product can provoke in protein inhabitation and reduce the expression of p53 mutants which act as oncogenes (Grajek *et al.,* 2005).

4.2 Potential preventive and therapeutic role of antioxidants

Antioxidants from fruit by-product exhibited therapeutic effects in opposition to cancer, oxidative stress, immunity problem, and microorganism that can cause disease including the reduction of cardiovascular diseases, capillary fragility, platelet aggregation, and so on (Rice-Evans, 2001). Particularly, the extract of fruit by-product (e.g., apple peel, rambutan peel, and date pit) contains phenolic compounds and flavonoids which can actively suppress the rapid growth of tumour cells (Wadhwa, 2016). Phenolic compound and flavonoids from apple peel extract sharply inhibited the rapid growth of tumour cells in the colon, date pit extract helps to deteriorate cytotoxicity of azoxymethane that induced colonic cancer (Wadhwa, 2016). Peel extract of yellow rambutan *(Nephelium lappaceum)* demonstrated anti-proliferative action against breast and osteosarcoma cancer (Emylia *et al.,* 2013). The extract of mango peel and seed kernel is widely used in pharmaceutical industries. (Jahurul *et al.,* 2015). These extracts contain penta-O-galloyl-glucoside (PGG) which possesses potential hydroxyl radicals and oxygen scavenging function; moreover, studies have revealed that PGG expressed multiple bioactivities involving beneficial effects towards the tumour, oxidative stress, and cardiovascular disease (Park *et al.,* 2008). Particular components from passion fruit skin demonstrated a strong bronchodilator effect by relieving bronchospasm in patients with asthma. Moreover, peel extract of purple passion fruit is considered to decrease the breathing difficulties in asthma patients especially adults during their oral administration (Wadhwa, 2016).

5. Synbiotics

A new concept has been introduced in biogenic known as synbiotics which is composed of probiotics and prebiotics. The dietary intervention with synbiotics aimed at correcting the breakdown of gut microbiota or subsequent imbalanced diets which may offer benefits for health by simplifying the weight reduction process (Sergeev *et al.,* 2020). Probiotics like *Lactobacilli, Bifidobacterium, Saccharomyces boulardii* and prebiotics such as galactooligosaccharides (GOS), xylooligosaccharides (XOS), fructo-oligosaccharides (FOS) and inulin are the most commonly used substances to produce synbiotics (Hernández-Alcántara *et al.,* 2016). The study revealed that synbiotic supplementation along with low-calorie diet programs exhibits salutary effects on the congelation of serum irritant markers and on excess fluid volume in breast cancer with lymphedema (Vafa *et al.,* 2020). The therapeutic potential of synbiotics includes antimicrobial and anticarcinogenic activity, antidiarrheal characteristics, defensive mechanisms against allergy, osteoporosis supersession, and immune system modulation (Manigandan *et al.,* 2012). Figure 1 illustrates the synbiotic applications with their mode of action (George Kerry *et al.,* 2018). Prebiotics and probiotic bacteria may impact metabolic activity on host health in diabetes by redirecting the autoimmunity, enhancing β-cell proliferation, and diminishing β-cell apoptosis (Patterson *et al.,* 2016). Synbiotics provide a significant contribution in the metabolic output by modulating the composition in human gut microbiota which play a key role in the therapeutic application against several health diseases, ranging from infant diarrhoea to adults inflammatory disorders (Gurry, 2017). Another study reported that synbiotic bread containing *Lactobacillus sporogenes* and inulin showed a significant reduction in the serum lipid profile triacylglycerol (TAG), high-density lipoprotein cholesterol (HDL-C), total cholesterol (TC), and insulin levels compared to control bread (Sáez-Lara *et al.,* 2016). The synergistic effect of synbiotic illustrated in Figure 2 which increases the growth of lactic acid to abate intestinal inflammation (Gurry, 2017).

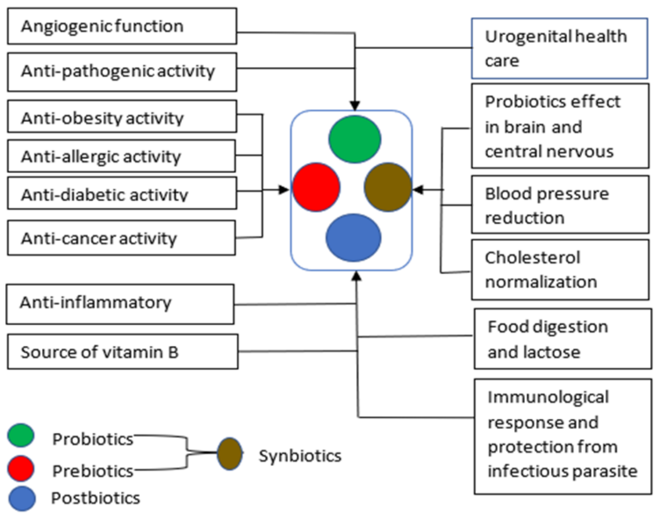

Figure 1. Synbiotic applications with their mode of action (George Kerry *et al.,* 2018)

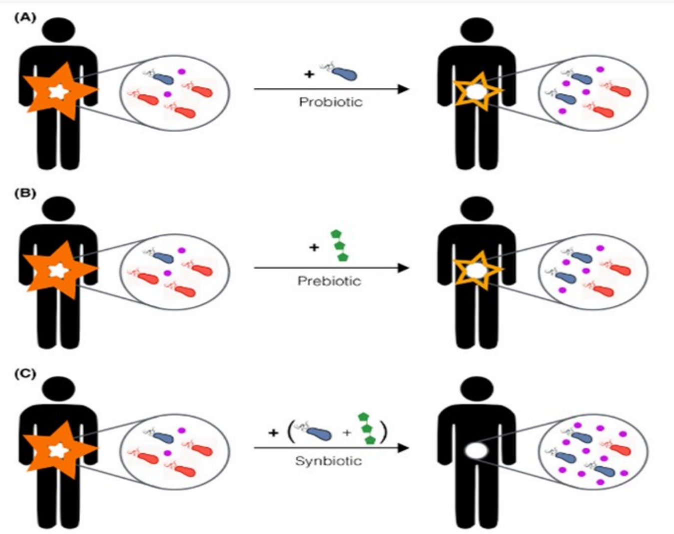

Figure 2. The synergistic effect of gut microorganisms (A) Administering of lactic acid (represented in purple color) producing probiotic (B) addition of prebiotic (C) synbiotic formulation (Gurry, 2017)

6. Probiotics

The term probiotic was explained by a Russian scientist namely Elie Metchnikoff for the first time, by suggesting the possibility of replacing bad microbes with beneficial ones at the beginning of the 20th century (Khare *et al.,* 2018). Metchnikoff also mentioned about the intake of fermented milk would "seed" the lactic acid bacteria and helps to reduce the outgrowth of proteolytic bacteria. Probiotic is live microorganisms that promote the intestinal microbial status and beneficially affect the host (Pandey *et al.*, 2015). Food and Agriculture Organization (FAO) and the World Health Organization (WHO) (FAO/WHO, 2001), defined probiotics as "live microorganisms when administered in adequate amounts confer a health benefit on the host". The mostly used probiotics genus is *Lactobacillus, Bifidobacterium, Saccharomyces, Enterococcus, Leuconostoc, and Bacillus* (Khare *et al.,* 2018). There are few characteristics of an ideal probiotic. First of all, the culture should be gram-positive, must express a positive effect on the host health, resistant to acid and bile salt, with a minimum colony-forming unit (CFU) of 30×109 per gram. Secondly, the culture should be strain-specific with longer survival rates and multiply rapidly in the digestive area. Lastly, they should be nontoxic to the host with the firm and faster adhesiveness ability of a microorganism (Khare *et al.,* 2018).

6.1 Mechanism of action of probiotics

Probiotics exhibit a lot of advantageous effects on the human body. For instance, probiotics can develop the existing microbial status in the gut area and balance the functional activities between bacteria and pathogens of the organism (Ta, 2010). Furthermore, probiotics can reduce the growth activity of harmful bacteria such as *Clostridium perfringens*, *Escherichia coli, Campylobacter jejuni, and Salmonella enteritidis* efficiently (Markowiak and Ślizewska, 2017). The way of action of probiotic includes strong epithelial barriers, mucosal adhesiveness properties, the prohibition of pathogen adhesion, competitive exclusion of pathogens, and immune system regulation. The intestinal barrier is the key defence system for maintaining epithelial integrity to save the organism from unfavourable conditions. The factors responsible to disrupt the barrier function are peptides (antimicrobial), Immunoglobulin A (IgA), and the epithelial junction adhesion while antigens from bacteria and food can influence the inflammation that may cause the intestinal disorders (Ohland *et al.,* 2010). The mechanisms of probiotics to increase the function of the intestinal barrier still not identified clearly. Studies have revealed that promoting gene expression for tight junction signalling can be a probable mechanism to amplify the mucosal barrier unity (Anderson *et al.,* 2010). Moreover, probiotics may have the ability to block pathogens by adhering with epithelial cells which exerts a beneficial effect for immune modulation by triggering the signalling cascade. The release of many soluble compounds from epithelial cells may contribute to direct/indirect activation of immune cells to prevent contagious diseases and the inflammation of the alimentary tract (Oelschlaeger, 2010). Organic acids generated by probiotics namely acetic and lactic acid can exert strong inhibitory action towards Gram-negative bacteria. The abovementioned acids are thought to be as principle antimicrobial components to fight against pathogens (Makras *et al.,* 2006). One Individual bacteria can decrease the activity of another species bacteria by subsequent mechanisms: formation of hostile microbial ecology, exclusion of attainable bacterial receptors, emission of antimicrobial components, and competitive reduction of necessary nutrients (Khare *et al.,* 2018).

6.2 Potential preventive and therapeutic role of probiotics

Studies have revealed the promising effect of probiotics on the development of strong immunity, protection against disease caused by infections or allergic substances, improvement in total antioxidant capacity (TAC) and plasma total glutathione (GSH) level (Gourbeyre and Denery, 2011; Roshan *et al.,* 2019). Figure 3 shows some properties of ideal probiotics (Khare *et al.,* 2018). Different studies have been conducted to determine the possible therapeutic application for disease prevention such as insulin resistance syndrome, type 2 diabetes, obeseness, and non -alcohol hepatic steatosis of probiotic microorganisms (Markowiak and Ślizewska, 2017; George Kerry *et al.,* 2018). Probiotic shows significant contributions in host metabolic processes, thus improve their health status by reducing the risk of metabolic diseases such as hypertension, obesity, cardiovascular diseases, arteriosclerosis, cancer and ageing. Probiotics are also responsible for qualitative alterations in intestinal mucus which prevent pathogen binding (Moayyedi *et al.,* 2010; Roy and Kumar, 2019). Moreover, pomegranate by-product increases the growth of probiotic bacteria such as *Bifidobacteria* and *Lactobacilli* have been confirmed to have potential anti-obese activity. Wang *et al.* (2019), studied the effects of probiotics in obese adults and reported that probiotics show beneficial effects on weight reduction with the changes in lipid profile and glucose metabolism. Another study suggested that probiotic diet play a preventive role in obesity establishment and reduce the risk of problems associated with obesity (Rouxinol-Dias *et al.,* 2016).

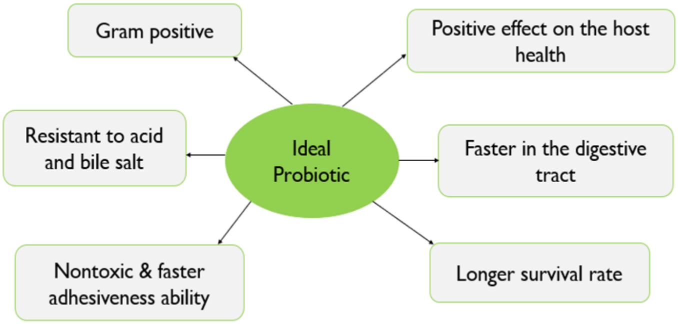

Figure 3. Properties of ideal probiotics (Khare *et al*., 2018)

7. Prebiotics

The term prebiotics was first commenced by Glenn Gibson and Marcel Roberfroid in 1995 and described as "a non-digestible food ingredient that beneficially affects the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon, and thus improves host health" (Gibson and Roberfroid, 1995). Concerning the definition, only a limited number of carbohydrate groups can be categorized as prebiotics such as fructo-oligosaccharides (FOS), inulin, galacto-oligosaccharides (GOS). In 2008, the International Scientific Association of Probiotics and Prebiotics (ISAPP) defined "dietary prebiotics" as "a selectively fermented ingredient that results in specific changes in the composition and/or activity of the gastrointestinal microbiota, thus conferring benefit(s) upon host health". A compound must have the following criteria to be classified as prebiotic: resistant to acidic pH in the stomach, do not absorb in the gastrointestinal tract, can be fermented by intestinal microbes, can stimulate the growth/activity of the intestinal bacteria to improve host's health (Davani-Davari *et al.,* 2019). The popular prebiotics is FOS, GOS, trans-galacto-oligosaccharides (TOS), Mannan-oligosaccharides (MOS), and inulin. Fruit by-products are a good source of carbohydrates with potential prebiotics (Ohshima *et al.,* 2016). Moreover, prebiotics can be synthesized from starch or carbohydrates utilizing apposite enzymes. In recent years, the production of functional foods with prebiotic components has exhibited dominant features in food factories and promising market value for economic reasons and scientific evidence of its well-being. The result has shown that during bio-therapeutic formula preparation, appropriate microbial strains and prebiotic ingredients can improve the viability of probiotics in the target site (colon and small intestine) (Ohshima *et al.,* 2016). Therefore, the increasing demand of health consciousness among consumers will offer remunerative opportunities for the prebiotic producer.

7.1 Mechanism of action of prebiotics

The intestinal microorganism works as a protector against very harmful bacteria by producing antimicrobial components and compete for epithelial attachment or nutrients (Schley and Field, 2002). By the fermentation, process prebiotics generates short-chain fatty acids (SCFAs) like propionic acid, lactic acid, and butyric acid which might have multiple advantages on human health (Davani-Davari *et al.,* 2019). For instance, butyrate can influence the development of intestinal epithelial. These acids are highly digestible substrates for bacteria. Besides, they show advantageous effects on metabolic activity, pH value, increase the length and number of the intestinal and epithelial villus, respectively (Khare *et al.,* 2018). Multiple surface determinants are displayed by prebiotics involving in the interaction process with intestinal epithelial cells (IECs) and mucus to prevent the adhesion of pathogenic bacteria (Khare *et al.,* 2018). Mannan-oligosaccharides (MOS), act by agglutination via the collaboration process of mannose sensitive lectins that are found in the cell wall surface of particular gram-negative bacteria and restrain colonization of pathogens by the attachment of digestive tract site (Heinrichs *et al.,* 2003). Another commonly used prebiotic namely inulin is not absorbed in the small intestine but can be fermented rapidly in other parts of the alimentary canal agitating proliferation of *Lactobacillus* and *Bifidobacterium* (Gibson and Roberfroid, 1995). A significant reduction of detrimental bacteria is also observed due to the changing effect of bifidogenic bacterial microbiota in the gut system. SCFAs produced by *Bifidobacteria* which can inhibit the proliferation and maintain low pH value with a concurrent hostile environment for pathogens. Furthermore, the proliferation caused by different species like *E. coli, Clostridium perfirgensis* and *Salmonella* can be repressed by several *Bifidobacteria* strains (Khare *et al.,* 2018).

7.2 Potential preventive and therapeutic role of prebiotics

Parra-Matadamas *et al.,* (2015) investigated the prebiotic activity of flour obtained from grapefruit, pear and pineapple peel in association with probiotic bacteria. Orange peel extract contains pectic oligosaccharides (POS) which expressed the prebiotic properties of increasing the number of *Bifidobacteria* and *Eubacterium rectale* with higher butyrate concentrations (Suárez *et al.,* 2010). Hamzaha *et al.* (2018), reported that grape pomace extract shows a significant role in intestinal tract microbiota and improve gastrointestinal health with the presence of *Lactobacillus acidophilus*. Together with the polyphenol contents, grape seeds contain a particular number of oligosaccharides and prebiotic activity is the most well-demonstrated action of oligosaccharides (Bordiga *et al.,* 2019). Agro-food by-product offers a golden opportunity in nutraceuticals and

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value-added foods. XOS produced from these by-product presents the prebiotic efficiency on host health by optimising the activity in the colon, metabolic process and immunomodulatory function (Samanta *et al.,* 2015). In addition, XOS can abate pro- carcinogenic enzymes, high pH value and nitrogenous waste. Resistant starch, which is unabsorbed in the gastrointestinal tract and oligosaccharides namely raffinose has been recognised as prebiotic carbohydrates that enhance the growth activity of good bacteria (Dwivedi *et al.,* 2014).

8. Conclusion

Fruit processing by-products are effective and less expensive natural sources of bioactive compounds. These are typically considered useless but contain known bioactive components that exhibit significant antioxidant and synbiotic properties. Thus, it can be alternative sources of natural antioxidants and other bioactive compounds. The by-products of various fruits, i.e., mango, banana, watermelon, grape, pomegranate, papaya and apple are considered optimal sources of antioxidant compounds, prebiotics which can be utilised as a growth media for beneficial microbial strains. Several articles have been summarised in this review to provided concise information associated with the possible therapeutic application of antioxidants and synbiotics in human health disease. Individually selecting probiotics and prebiotics is a pre-requisite for synbiotic combination to maximise the synergic and beneficial effects. Antioxidants and prebiotics from by-products have multifactorial effects on the host health by improving the intestinal environment and metabolic process with negligible side effects. As a result, these can be used as less expensive but effective sources of healthcare supplements. This summery also illustrated the potential therapeutic applications including modes of action of bioactive compounds, which can be a useful guideline for future researchers. The present study recommends that further research should address toxicity and the effects of the long-term dietary intervention of synbiotics before clinical.

Conflict of interest

The authors declare they have no conflict of interests.

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