The Pharma Innovation Journal 2023; 12(7): 1860-1869

www.ThePharmaJournal.com

The Pharma Innovation

ISSN (E): 2277-7695
ISSN (P): 2349-8242
NAAS Rating: 5.23
TPI 2023; 12(7): 1860-1869

www.thepharmajournal.com
Received: 19-05-2023
Accepted: 27-06-2023

Rushikesh Subhash Pharate
Department of Food Technology and Nutrition, School of Agriculture, Lovely Professional University, Phagwara, Punjab, India

Komal Dadasaheb Barguje
Department of Microbiology, Savitribai Phule Pune University, Pune, Maharashtra, India

Prajakta Subhash Pharate
Department of Microbiology, Vidya Pratishthan's Arts Science and Commerce College Baramati, Pune, Maharashtra, India

Corresponding Author:
Rushikesh Subhash Pharate
Department of Food Technology and Nutrition, School of Agriculture, Lovely Professional University, Phagwara, Punjab, India

A review on bioactive compounds from different fruit waste materials: Classic and novel extraction technique, health benefits

Rushikesh Subhash Pharate, Komal Dadasaheb Barguje and Prajakta Subhash Pharate

DOI: https://doi.org/10.22271/tpi.2023.v12.i7v.21502

Abstract
Fruit waste is a major byproduct of the food industry and its disposal causes serious environmental problems. However, fruit waste is also a rich source of bioactive compounds such as polyphenols, carotenoids, and flavonoids that have potential health benefits. This review paper aims to provide a comprehensive overview of the extraction techniques used for the recovery of bioactive compounds from fruit waste, their health benefits, and their applications. The paper also discusses future perspectives and recommendations for the effective utilization of fruit waste. The paper discusses different extraction techniques such as conventional and non-conventional employed in different fruit waste materials. The health benefits section highlights the potential of bioactive compounds from fruit waste in the prevention and treatment of various diseases such as diabetics, cancer, cardiovascular diseases, and diabetes. This review emphasizes the recommendations such as optimizing the extraction conditions to maximize the recovery of bioactive compounds and the need for further research to explore the potential of fruit waste-derived bioactive compounds in various fields. In conclusion, this review provides a comprehensive overview of the extraction techniques, health benefits, and applications of bioactive compounds from fruit waste. The paper highlights the potential of fruit waste-derived bioactive compounds as a sustainable source of valuable compounds for various industries.

Keywords: Bioactive compounds, novel extraction, conventional extraction, fruit shells, fruit waste

1. Introduction

At a global scale, food industry by-products represent a critical source of pollution: food losses and waste occur throughout the food supply chain, accounting for around 1.3 billion tons per year, or 16% of the total food supply (Marcillo-Parra *et al.*, 2021) [56]. A wide range of by-products come from fruit processing, particularly from the juice industry, including peels, unusable pulp, seeds, and fruit shells a large amount of this material is ultimately discarded. The conversion of these wastes into high-value food products could mitigate losses by increasing demand for post-harvest and agro-industrial by-products that can be used as sources of bioactive compounds with antioxidant properties and applied in the development of functional products. Most fruits produce at least a minimum of 25–30% of byproducts in the form of peel, seed, pomace, etc. (Sagar, Pareek, Sharma, Yahia, & Lobo, 2018) [17]. Several studies on fruit by-products in the form of peels, seeds, pomace, and shell extracts have found a wide variety of bioactive compounds, such as phenolic acids, flavonoids, anthocyanins, carotenoids, and vitamin C. In fruits, "bioactive compounds" are those secondary metabolites typically produced in small amounts along with primary metabolites such as proteins, carbohydrates, and lipids. These secondary metabolites are supposed to assist the plants in increasing its overall capability to survive (resistance against ecological stress, diseases, and UV radiation) and allow them to grow. These bioactives are recognized to exhibit antioxidant potential, anti-microbial, anti-cancer or anti-inflammatory capacities thus, helping to prevent oxidative stress and related chronic diseases. Therefore, it is necessary to utilize this bioactive rich waste by extracting them using several conventional extraction methods such as hydrodistillation, soxhlet extraction and maceration and greener and less hazardous novel techniques such as ultrasound-assisted extraction, supercritical fluid extraction, microwave-assisted extraction and enzyme-assisted extraction etc.

Present review summarizes the novel green extraction techniques and conventional extraction methods for bio-actives from various fruit waste materials, with their principle and mechanism. This review attempted to include recent research papers on various health benefits of different fruit materials. This information will be helpful to the industry personnel, academia, and researchers, whose intention is to develop food products with natural bio-actives and with an objective of green labels.

2. Extraction of bio-active compounds from fruit waste materials

Fruit waste materials are rich sources of phytochemicals and have been extensively investigated for their content of phenolic compounds, dietary fibers, and other bioactive substances. While the pulp of most fruits is commonly consumed, research has demonstrated that significant quantities of phytochemicals and essential nutrients are present in the seeds, peels, and other components of fruit that are typically (Rudra *et al.*, 2015) [18]. Investigators have explored a variety of conventional (e.g., hydro-distillation, Soxhlet extraction, maceration) and non-conventional (e.g., ultrasound-assisted extraction, supercritical fluid extraction, microwave-assisted extraction, enzyme-assisted extraction) techniques for the isolation of bioactive constituents from fruit byproducts. It has been determined that non-conventional methods offer several benefits over conventional approaches, including lower production costs, shorter processing times, reduced solvent usage, eco-friendliness, higher extraction yields, and decreased energy consumption and CO2 emissions (Jiang *et al*., 2021) [19].

2.1. Conventional extraction methods

2.1.1. Hydro-distillation

Hydro-distillation involves combining solid material with water and subjecting it to distillation using an electric heating mantle. This process allows for the condensation and recovery of volatile compounds (Chen *et al*., 2021) [1]. However, hydro-distillation has its drawbacks, including the loss of certain components, natural pigments, and heat-sensitive bioactive compounds due to the high temperatures used, which exceed the boiling point of water (Aramrueang *et al*., 2019) [2]. This method has been employed to extract essential oils and hydrosols containing significant volatile compounds from pineapple and pomegranate peels (Mohamad *et al*., 2019; Ara & Raofie, 2016) [4, 3]. Researchers have introduced a novel approach that employs solar hydro-distillation as a zero-waste biorefinery technique to isolate essential oils, polyphenols, and pectins from orange peel. The findings of this research indicate that TPC (total phenolic content), TFC (total flavonoid content), hesperidin, narirutin, and pectin remain in the peels after extraction with high retention levels, especially after solar hydro-distillation (Hilali *et al*., 2019) [5].

2.1.2. Soxhlet extraction (SE)

The Soxhlet extraction method involves a small quantity of dry sample, which is placed on the soxhlet extractor where the solvent flows through. The procedure is repeated until the extraction is accomplished. This method necessitates prolonged extraction time and substantial amounts of solvent (Soquetta *et al*., 2018) [7]. The key parameters that affect the Soxhlet extraction process are the type of solvent and its qualities. Lipophilic chemicals and pigments such as carotenoids and chlorophyll are extracted using low-polar solvents like petroleum ether and chloroform. A research study used the Soxhlet technique with pure ethanol to extract TPC from sweet variety tamarind seeds and obtained 387.4 GAE/g extract (Reis *et al*. 2016) [6].

2.1.3. Maceration

The research study investigated the tangerine peels, researchers observed that the maximum extraction of TPC was obtained (28 mg GAE/g extract) by maceration at a temperature of 40 °C when using 80% methanol as the extracting solvent (Safdar *et al*., 2017) [8]. According to a comparative study, the antioxidant potential of Jackfruit (AhJ33) waste extracts (rind and rachis) was evaluated using three different extraction methods: maceration, percolation, and Soxhlet. The results indicated that for both rind and rachis, the maceration technique yielded extracts with the highest antioxidant activities. This was found to be correlated with the highest TPC and TFC values (Daud *et al*., 2017) [9].

2.2. Green/Novel extraction methods

2.2.1. Microwave-assisted extraction (MAE)

Microwave-assisted extraction (MAE) is an innovative method for extracting bioactive compounds from fruit waste. This technique involves heating solvents containing plant samples using microwave energy, which facilitates the transfer of analytes from the sample matrix into the solvent. When microwave radiation passes through the solvent and sample, it is directly converted to the solid sample without being absorbed by the solvent. This results in rapid heating of the moisture within the solid sample, leading to evaporation and the generation of high vapor pressure. The high vapor pressure causes the cell walls of the sample matrix to rupture, releasing the desired components into the solvent (Sonar *et al*., 2020) [15]. The efficacy of Microwave-Assisted Extraction (MAE) is contingent upon several parameters, including microwave power, solvent properties, extraction duration, temperature, sample composition, and the dielectric constants of the target compounds. Research data indicates that the MAE process was utilized to extract betalain from dragon fruit peel. Under optimal conditions of 35 °C and an 8-minute treatment duration, a betalain yield of 9 mg/l was obtained from a 20 g sample (Sabrina *et al*., 2023) [16]. A recent research study has investigated the recovery of polyphenolic compounds from ripe mango peel using an MAE with deep eutectic solvents (DES). The lactic acid/sodium acetate/water (3:1:4) was DES system and used as the extractant. The optimal conditions were determined as 436.45 W, 19.66 min, and a liquid-to-solid ratio of 59.82 mL g^{-1}. Under optimal conditions, the recovery of TPC was 56.17 mg gallic acid equivalent g^{-1} dw. The researcher identified mangiferin as the prominent phenolic compound in the mango peel extracts. Researchers concluded that MAE with DES extraction had remarkable effects on the extraction efficiency of phenolic compounds (Pal *et al*., 2020) [10].

2.2.2. Supercritical fluid extraction method (SFE)

Supercritical Fluid Extraction (SFE) is a highly effective method for isolating natural bioactive compounds such as flavonoids, essential oils, seed oils, carotenoids, and fatty acids from fruit waste materials. It is considered a sustainable alternative to conventional extraction techniques (More *et al*., 2022) [20]. It is a technique that employs a supercritical fluid (SCF) as a solvent to extract and separate substances. A supercritical fluid is formed when a fluid is subjected to pressure and temperature above its critical point, causing the liquid and gas phases to become indistinguishable. Supercritical fluids exhibit the physicochemical properties of both liquid and gas states (Khaw *et al*., 2017) [21]. A variety of compounds have been investigated for their potential as supercritical fluids (SCFs), including hydrocarbons (pentane, butane, hexane), aromatics (benzene, toluene), alcohols (methanol, isopropanol, n-butyl alcohol), and gases (carbon dioxide, ethylene, propane) (Uwineza & Waskiewicz, 2020) [22]. The SFE process comprises two critical stages: extraction and separation. Both solid and liquid samples may be utilized, depending on the system configuration, but solid samples are more commonly employed. In the case of solid samples, columns are packed with pre-treated (dried and milled) samples, and pressurized supercritical solvents flow through the column, dissolving extractable compounds from the solid matrix. The dissolved compounds are transported via diffusion to the separator, where the extract and solvent mixtures are separated by altering the pressure (Boyacı *et al*., 2015) [23]. Research data demonstrated that SFE of β-carotene from enzyme-treated ripe bitter melon pericarp resulted in a maximum yield of 90.12%. This was achieved by applying a pressure of approximately 390 bar, a flow rate of 35 mL/min, a temperature of 70 °C, and an extraction time of 190 min to lyophilized enzymatic pretreated ripe bitter melon pericarp (Patel *et al*., 2019) [24]. Supercritical Fluid Extraction (SFE) has also been employed to recover phenolics from grape bagasse derived from pisco residues. The optimal extraction conditions were determined to be 40 °C, 20–35 Mpa for 180 minutes using 10% ethanol (w/w). The compounds identified in the extracts included syringic, vanillic, gallic, p-hydroxybenzoic, and p-coumaric acids, as well as quercetin (Farías-Campomanes *et al*., 2013) [25]. A recent study examined the extraction of bioactive compounds from pomegranate (*Punica Granatum* L.) fruit peels using various methods, including Cold Maceration (CM), Ultrasonic Extraction (UE), Soxhlet Extraction (SE), and Supercritical Fluid Extraction (SFE). Methanol, ethanol, and acetone were used as solvents in conventional extractions, while the operating pressure was varied (10, 15, 20, 25 MPa) in SFE. The researchers concluded that the SFE extract obtained at 20 MPa contained the highest content of total polyphenols (11,561.84 µg/g), with ellagic acid being the predominant compound (7492.53 µg/g) (Kupnik *et al*., 2022) [11].

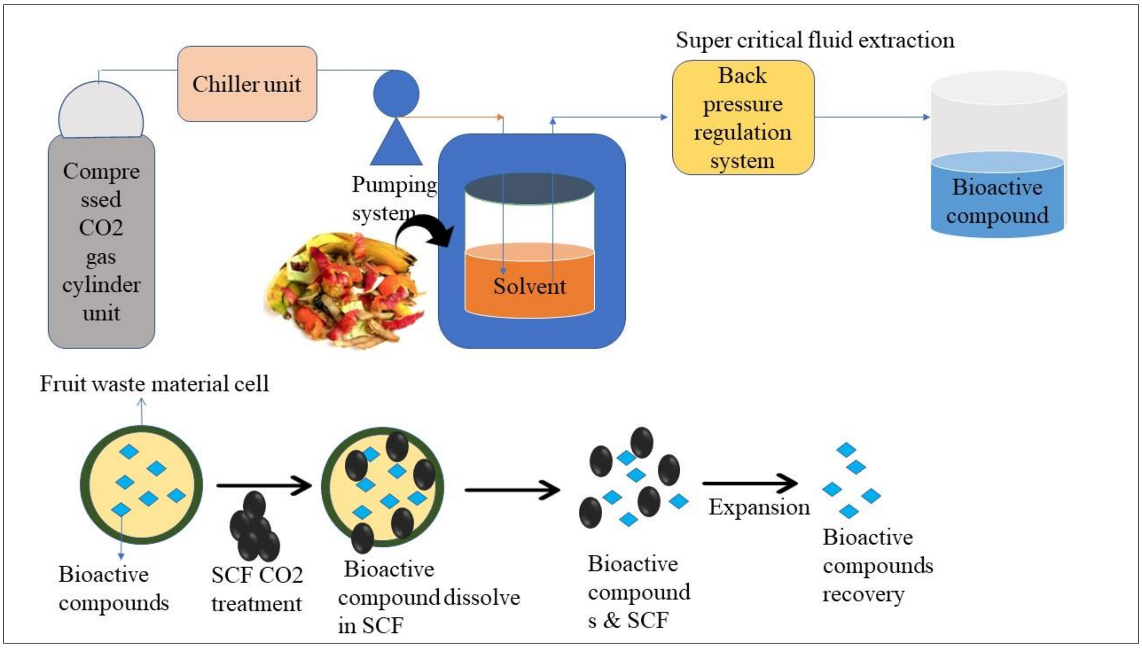

Fig 1: Super critical fluid extraction.

2.2.3. Ultrasound-assisted extraction (UAE)

Ultrasound-Assisted Extraction (UAE) is a modification of conventional extraction methods designed to increase yield at a lower cost. In the UAE process, ultrasound waves are employed to enhance efficiency through cell disruption and effective mass transfer (Kumar *et al*., 2020) [29]. In this extraction technique, mechanical energy generated by ultrasound waves is applied to the samples. This sonication results in cavitation, the formation of small vacuum bubbles or voids in the liquid, which implodes upon contact with the solid sample, producing localized high temperatures (approximately 4500 °C) and pressures (approximately 50 MPa). These forces induce effects such as sonolysis, destruction of cell membranes, and extraction of intracellular material. UAE can be subdivided into direct and indirect methods. In direct UAE, a sonotrode is immersed in the sample-solvent mixture and ultrasonic radiation is applied directly. In indirect UAE, ultrasonic radiation is applied to the sample-solvent mixture via an ultrasonic bath, which can accommodate multiple samples simultaneously (Chavan *et al*., 2022) [26]. Bioactive compounds, including polyphenols, flavonoids, and carotenoids, were extracted from bael fruit pulp waste using the UAE technique. Response Surface Methodology (RSM) optimization of the extraction process variables yielded an ethanol concentration of 51.22%, an ultrasound amplitude of 51.45%, and an ultrasound treatment time of 6.11 minutes. The investigators determined that the utilization of UAE methodology for the isolation of bioactive constituents from fruit byproducts is feasible for large-scale production in the development of food additives and pharmaceuticals (Sonawane *et al*., 2020) [27]. The investigators have shown that the most favorable parameters for the UAE of bioactive constituents from orange peel were a power output of 400W, an extraction duration of 30 minutes, and a solvent composition of 50% ethanol in water. Under these conditions, the total carotenoid content was determined to be 0.63 mg ß-carotene/100 g, the vitamin C content was 53.78 mg AA/100 g, and the phenolic content was 105.96 mg GAE/100 g. Hesperidin was identified as the predominant phenolic compound in all orange peel extracts, with a maximum concentration of 113.03±0.08 mg/100 g (Montero-Calderon *et al*., 2019) [28]. A study was conducted to compare the efficacy of UAE, MAE, and maceration for the isolation of phenolic constituents from ciriguela peel. The phenolic extract obtained using optimized UAE was found to have a higher yield and greater antioxidant activity (35.15 mg GAE/g, IC_{50} = 0.19 mg/mL) compared to conventional extraction (30.10 mg GA/g and IC_{50} = 1.68 mg/mL) and MAE (23.31 mg GA/g and IC_{50} = 4.29 mg/mL). The investigators concluded that UAE was the most effective and efficient method for obtaining bioactive extracts from ciriguela residue (Junior *et al*., 2021) [12].

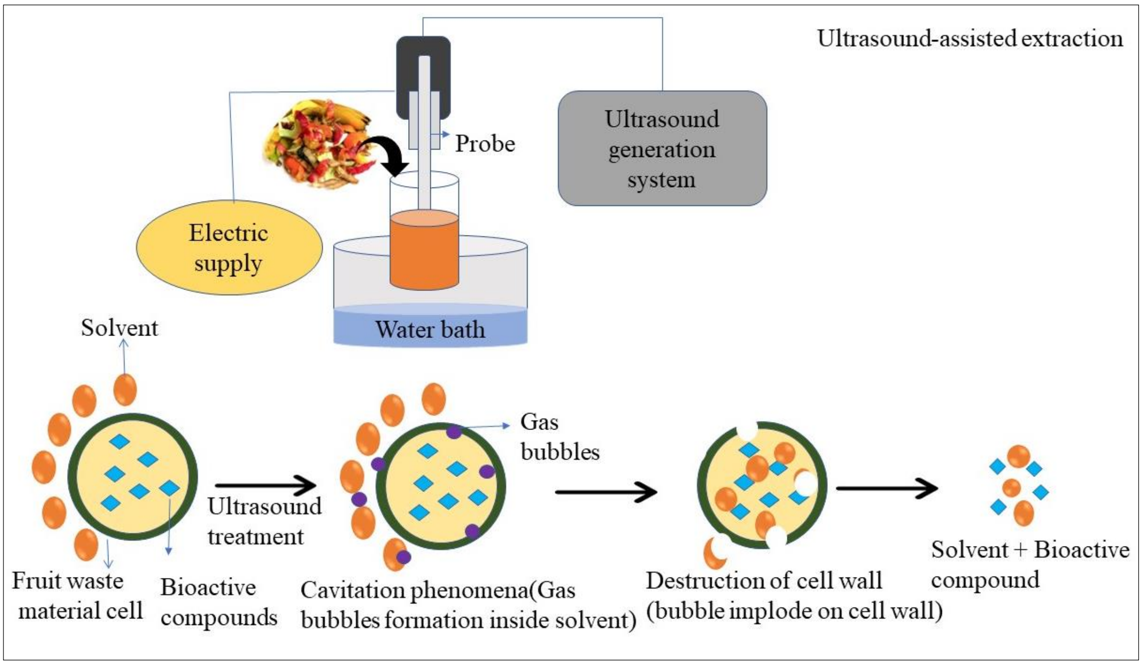

Fig 2: Ultrasound-assisted extraction

2.2.4. Enzyme-assisted extraction (EAE)

Enzyme-assisted extraction (EAE) has emerged as an innovative and effective approach for the release of bound compounds and the enhancement of overall extraction yields. The incorporation of specific enzymes, such as cellulase, α-amylase, and pectinase, during extraction, facilitates the recovery of target compounds by degrading cell walls and hydrolyzing structural polysaccharides and lipid bodies. Two approaches to EAE have been developed: enzyme-assisted aqueous extraction (EAAE) and enzyme-assisted cold pressing (EACP). EAAE methods, which utilize water as the extraction medium, have been primarily employed for the isolation of oils from various seeds. In contrast, EACP involves the use of enzymes to hydrolyze seed cell walls in the absence of a polysaccharide-protein colloid, which is present in EAAE. Key factors influencing the efficacy of EAE include enzyme composition and concentration, plant material particle size, solid-to-water ratio, and hydrolysis duration (Sánchez-Camargo *et al*., 2020; Selvamuthukumaran & Shi, 2017) [13] (Gligor *et al*., 2019) [14, 30]. A research study has demonstrated that developed raspberry pomace press cake contains 30-35% lipophilic compounds, including essential fatty acids, tocopherols, phytosterols, and ellagitannins. The EAAE was employed to recover lipophilic compounds and polyphenols from raspberry pomace press cake. Under optimized conditions (1.2 units of thermostable alkaline protease/100 g PPC, pH 9, 60 °C, and 2 hr hydrolysis), over 38% of the total lipophilic content of pomace pressed cake was recovered in the aqueous medium. The recovery of polyphenols and antioxidant activity was 48% and 25% higher, respectively than that achieved using a methanol/acetone/water extraction mixture (N Saad *et al*. 2019) [31].

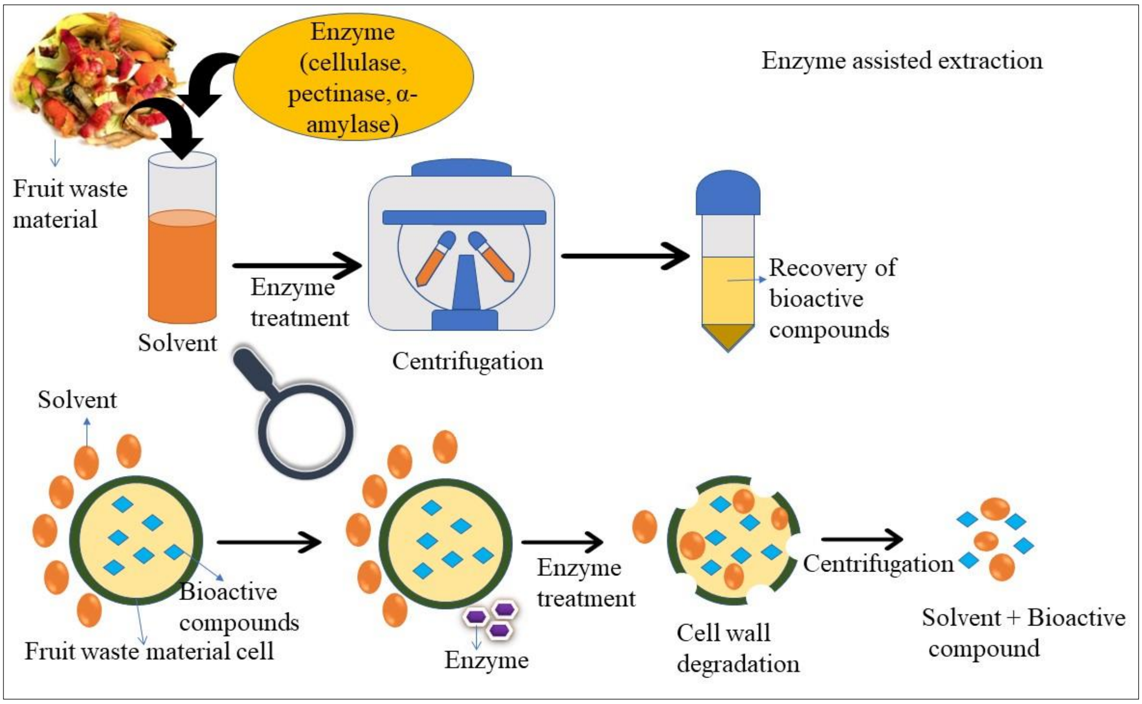

Fig 3: Enzyme-assisted extraction

Name of fruit	Extraction technique	Bioactive compounds	Extraction condition	Key finding	References
Avocado Pulp	Cold-pressing Soxhlet extraction	a-tocopherol squalene b-sitosterol	Cold pressing Soxhlet extraction (petroleum ether)	• Oil obtained by cold pressing was 25–33% • Oil obtained by Soxhlet extraction was 45–57% • Levels of a-tocopherol, squalene and b-sitosterol decreased during pulp drying of avocado.	Lefebvre *et al.*, 2021 [57]
Pumpkin (seed and shell)	Freeze drying Oven drying	Phenolic acids	Solvent extraction (70% ethanol, 70% methanol, 70% acetone, Ultra-pure water, 100% dichloromethane	• The solvents 70% ethanol and 70% acetone were the most efficient in the extraction of total phenolics, also with the highest antioxidant activity values. • The oven-dried samples showed higher phenolics and antioxidant activity values	Saavedra *et al.*, 2013 [58]
Chestnut shell	Microwave Assisted Extraction	Phenols	Extraction carried out by 50% aqueous methanol, and 50% aqueous ethanol Temperature: 25, 50, and 75 °C Time: 60–120 min.	• Retention of bioactive compounds. • Improved activity of antioxidants from extract of chestnut. • Extracts of chestnut shell and bur were able to inhibit the growth of gram positive and negative bacteria.	Vella *et al.*, 2017 [59]
Cocoa Bean shell	Pulsed Electric Field	Polyphenols Methylxanthines	Pre-treatment By using Methanol (≥ 99.9%), formic acid (98–100%), hydrochloric acid (fuming 37%), 6-hydroxy-2,5,7,8-tetramethylchroman2-carboxylic acid	• PEF-assisted technology to improve the recovery of bioactive compounds in CB (20%) • Extract had high phenolic and high anti-oxidant activity	Barbosa-Pereira *et al.*, 2018 [60]
Mango peel	Microwave-assisted	Phenolic compounds	conventional ethanolic extraction techniques by using ethanol, prepared in weight-per-weight proportions (0%, 10%, 25%, 50%, 75%, 100%), were used as solvent for extraction.	• Microwave-assisted extraction of mango reported to retain maximum antioxidant property. • Retention of phenolic compounds linearly correlated antioxidant activity.	Sánchez-Camargo *et al.*, 2021 [61]
Peanut shell	Ultrasound-Assisted Extraction (UAE)	Polyphenols	By using Ethanol and ascorbic acid	• UAE extraction of peanut shell retained the bioactive compounds. • Due to increased activity of tyrosinase and collagenase activity, these extracts from UAE helps in skin whitening and reported to produce anti-wrinkle properties.	Gam *et al.*, 2021 [62]
Pomogranate	Ultrasound	Phenolics,	Around 10 g sample of	• TPC increased slowly with the increase of	Sharayei *et*

Peel	assosted extraction (UAE)	flavonoids and pro-anthocyandins	Pomogranate Peel in form of powder was placed in the 100 mL flask, to which 40 ml of distilled water (1:4 w/v) was added, and then it was treated with UAE which was carried out at power 400 W and frequency 20 KHz.	UAE, and nearly reached a peak at 60% UAE. • Increase in phenolic content simultaneously cause the possibility to increase antioxidant activity.	*al*., 2019 [63]

3. Health benefits of Bioactive compounds
3.1 Antioxidant properties:
Fruits are widely consumed around the world because they have a variety of medicinal characteristics that work against a number of human disorders. Antioxidants are abundant in the majority of fruit species. According to research by Feng *et al*. (2018) [34], chemicals discovered in durain shells have a strong potential to scavenge DPPH free radicals as well as glycosides and triterpenoids. Nitric oxide (NO) formed by mouse RAW264.7 cells when LPS is present also has strong inhibitory effects on NO, and some phenolic compounds have a higher inhibitory effect on NO than indomethacin (Feng *et al*., 2016) [33].

In a study by Lameirao *et al*. (2020) [35], the synthetic antioxidant Trolox and the Chestnut shells (CS) extract generated using the UAE approach were compared. The findings revealed that CS extract has greater antioxidant activity than Trolox. Additionally, Pelvan *et al*., 2018 [36] found that CS extract has greater antioxidant activity than other nut by-product extracts such as walnut shells, hazelnut peels, and almond hulls.

Methanol, ethanol, ethyl acetate, acetone, hexane, and petroleum ether were employed by Arumugam *et al*. (2022) [38] to extract bioactive chemicals from groundnut shell and analyse the extracts using GC-MS. The primary chemicals found in the extracts included octadecane, palmitic acid, oleic acid, and lupeol. High-est antioxidant activity were obtained by the methanolic extract, with IC_{50} values of 789.36 g/mL for DPPH and 480.11 g/mL for ABTS. In contrast to other extracts, methanolic extract showed a minimum inhibitory concentration (MIC) of 250 g/mL against Aeromonas hydrophila, Klebsiella pneumoniae, Pseudomonas aeruginosa, and Staphylococcus aureus. According to the study, groundnut shells are a source of antioxidants and antibacterial chemicals that have a variety of uses.

In kabau shell extract prepared by maceration technique, Riasari *et al*. (2019) [37] assessed the antioxidant activity and phenol levels with IC_{50} values of seed shell from Lampung being 17.61 g/ml and those from South Sumatra being 44, 7 g/ml. Lampung's seed shells had a phenol content of 11.74 g GAE per 100 g and South Sumatra's had 5.88 g GAE per 100 g. Based on the research, it can be said that shell extract made by macerating shell from Lampung and South Sumatra included significant amounts of total phenol and antioxidant activity.

3.2 Antimicrobial Property-
Based on the inhibitory effects on the growth of Gram-positive (*Bacillus cereus, Bacillus subtilis*, *Staphylococcus aureus*, and *Staphylococcus epidermidis*) and Gram-negative bacteria (*Bacillus aureus*, *Bacillus subtilis*, and *Staphylococcus epidermidis*), Fernandez-Agull'o *et al*. (2014) [39] demonstrated the antibacterial activity of aqueous extracts (*Escherichia coli* and *Pseudomonas aeruginosa*). In comparison to bur extract, Castanea sativa shells demonstrated superior antibacterial activity against all tested microorganisms, obtaining minimum inhibitory concentrations (MIC) of 2.5 mg/ml.

The high antibacterial efficacy of CSS against microorganisms with multidrug resistance was demonstrated by Silva *et al*. in 2020 [41]. For instance, inner shells were more effective than outer shells, having lower MIC values (25-50 mg/mL) and being active against 6 of the 10 bacteria tested, including all Gram-positive bacteria (*S. epidermidis, S. aureus, Enterococcus faecalis*, and *Nterococcus faecalis*) and two Gram-negative bacteria (*Klebsiella pneumoniae* and *P. aeruginosa*). Conversely, just 3 bacteria were resistant to outer shells (*S. epidermidis*, *S. aureus* and *P. aeruginosa*). Salmonella enteritidis and *E. coli* were unaffected by either the inner or outer shells, while *S. epidermidis* was the target of the highest inhibitory efficacy. Regarding Gram-negative bacteria, the limited efficacy of natural extracts against these bacteria can be attributed to the lipopolysaccharide (LPS) from cells' surface-repelling polyphenols, which creates a significant barrier against the entry of polyphenols. Nonetheless, *K. pneumoniae* and *P. aeruginosa* were effectively inhibited by the inner and outer shells, with MIC values of 50 and 75 mg/mL, respectively. The inner and outer shells of chestnuts were also resistant to *Listeria monocytogenes*, *B. cereus*, *E. coli*, and *S. enteritidis*. The phenolic acids were credited in the concluding remarks with giving CSS its antibacterial effects against Gram-negative bacteria.

The antibacterial effectiveness of several formulations containing four plant extracts, including Acacia catechu, Ephedra sp., CSS, and Mumiyo, assessed by Dashtdar *et al*. (2013) [40]. Gram-positive (*S. aureus* and *S. pneumonia*) and Gram-negative bacteria responded most favourably to a formulation containing 25% CSS extract (*E. coli*, *K. pneumonia*, *Proteus mirabilis* and *P. aeruginosa*). Apart from *S. pneumonia*, this formulation also produced better results than povidone-iodine (50%) solution. Its potential utility as novel antiseptic agent in the treatment of acute or chronic skin ulcers, as well as evidence of its ethnopharmacological benefits against diarrhoea, venereal, and infectious disorders, may be supported by the synergistic effects between all extracts (Dashtdar *et al*. 2013) [40].

3.3 Anticancer property:
In comparison to traditional chemotherapeutic medications, a number of polyphenol-rich extracts from natural matrices have been proposed as prospective anti-cancer agents with selective Cytotoxicity for specific cancer cells. On a normal prostate cell line (PNT2) and six human cancer cell lines, including three prostate (DU 145, LNCaP, and PC-3), two breast (MCF-7 and MDA-MB-231) and one hepatocellular cancer cell (Hep G2), Cacciola *et al*. (2019) [42] evaluated the effects of various concentrations (1-100 g/mL) of CSS aqueous extract. The scientists noted that after exposure to the extract, the viability of DU 145 (IC_{50} = 35.78 g/mL), PC-3

(75% at 100 g/mL), LNCaP (IC_{50} = 54.88 g/mL), and MCF-7 cells (70% at 100 g/mL) drastically decreased, highlighting the cytotoxic effects of CSS extract on these cell lines.
Numerous tumour cells have been demonstrated to be inhibited from proliferating by various pomegranate plant sections. Pomegranate extracts were shown by Lee *et al*. 2010 [43] to be effective in preventing RAW 264.7 macrophage cells from producing NO. Additionally, it was discovered that pomegranate greatly reduced carrageenan-induced mice paw oedema for up to 5 hours.
According to Lansky *et al*. (2005) [44], extremely aggressive human prostate cancer PC-3 cells had their cell proliferation suppressed by pomegranate fruit extract, which was then followed by apoptosis. The possible anticancer processes of pomegranates have been clarified by numerous animal research. Pomegranate fruit extract (PFE; edible sections of the fruit, excluding the peel), according to two studies in mice implanted with the prostate cancer PC-3 cell line, slows cell growth and promotes apoptosis through modification of proteins regulating apoptosis (Malik *et al*., 2006) [45].
Avocado demonstrates intriguing qualities that point to its possible use in cancer treatment and prevention. In this situation, prostate cancer cell lines (Lu *et al*., 2005) [46], peripheral blood mononuclear cells, oesophageal squamous cell carcinoma, and colon adenocarcinoma cell lines all saw growth inhibition from avocado pulp extracts.
According to Butt *et al*. (2006) [47], persin, an oil-soluble chemical produced in avocado leaves and pulp, caused human breast cancer cell lines (MCF-7 and T-47D cells) to enter the G2-M cell cycle and undergo caspase-dependent apoptosis.

3.4 Antidiabetic effect
Nogueira and Pereira provided the first explanation of the PP's antidiabetic effects using an *in vivo* model. This was followed by Zafar and Singh and Nozire and Serpil, which were both replicated by numerous other research (1, 2, 3, 4).
Diabetes-prone rats received 0.43 g/kg B.W. of aqueous peel extract for four weeks, and the results showed considerably decreased blood sugar levels and an increase in beta cells, which are thought to assist intensify insulin levels. The extract's mechanistic anti-diabetic activity involves stimulating, regenerating, and increasing the number of cells, shielding pancreatic tissue, and causing the release of insulin as a result. Additionally, it might boost insulin receptor stimulation and activity (5).
The first proof that avocados can be used to treat diabetes was found in a screening research with adult male rabbits that was published by Alarcon-Aguilar *et al*. (1998) [52]. Aqueous seed extract (intragastric therapy) was seen to ameliorate hyperglycemia following an oral glucose excess (6).
When orange peel extract was tested for anti-diabetic properties in insulin-resistant diabetic rats, it was discovered to be quite effective (Sathiyabama *et al*., 2018) [53]. According to Tsutsumi *et al*. (2014) [54], the sudachitin (5,7,4′-trihydroxy-6,8,3′-trimethoxyflavone) PMF found in sudachi (*C. sudachi*) peel has anti-diabetic and anti-obesity properties.
According to Tsutsumi *et al*. (2014) [54], the sudachitin (5,7,4′-trihydroxy-6,8,3′-trimethoxyflavone) PMF found in sudachi (*C. sudachi*) peel has anti-diabetic and anti-obesity properties.

3.5 Anti-inflammatory activities
Donatella *et al*., (2019) [64] used kiwifruit peel extract to explore the anti-inflammatory potential. Procyanidins made up the majority of the polyphenols in the extract, accounting for 92% of the total by weight, according to analytical data. The extract prevented activated monocytes from producing pro-inflammatory cytokines such as IL-6, IL-1, TNF-, the danger signal HMGB1, and granzyme B serine protease. Western blot examination revealed an inhibitory activity of 81%, 68%, 63%, 76%, and 60% on the extracellular release of IL-6, IL-1, TNF-, HMGB1, and granzyme B, respectively. Additionally, the extract increased autophagy and stopped STAT3 activity.

4. Future perspectives
Based on the current literature, some recommendations can be made for future research and development on bioactive compounds from fruit waste. First, more studies are needed to evaluate the safety, stability, bioavailability, and efficacy of bioactive compounds from fruit waste *in vivo* and in human trials. Second, more efforts are required to optimize the extraction parameters and scale up the novel extraction techniques for industrial applications. Third, more attention should be paid to the valorization of the residual biomass after extraction, such as using it as animal feed, fertilizer, or biogas. Fourth, more collaboration and coordination are needed among different stakeholders, such as farmers, processors, researchers, and policymakers, to promote the sustainable utilization of fruit waste and its bioactive compounds.

Conclusion
Fruit waste is a major source of bioactive compounds that have various health benefits and applications. Research data has shown that conventional extraction techniques are often inefficient, costly, and environmentally unfriendly for bioactive compound extraction. Therefore, there is a need for alternative extraction methods that can recover bioactive compounds from fruit waste sustainably and effectively. This review summarizes the current knowledge on the types of bioactive compounds from fruit waste, such as polyphenols, carotenoids, pectins, and essential oils. It also discusses the different extraction techniques that have been used or proposed for fruit waste valorization, such as microwave-assisted extraction, ultrasound-assisted extraction, supercritical fluid extraction, and enzyme-assisted extraction. Moreover, it highlights the potential health benefits and applications of bioactive compounds from fruit waste in food, pharmaceutical, and cosmetics.

References
1. Chen G, Sun F, Wang S, Wang W, Dong J, Gao F. Enhanced extraction of essential oil from *Cinnamomum cassia* bark by ultrasound-assisted hydrodistillation. Chinese Journal of Chemical Engineering. 2021;36:38-46. https://doi.org/10.1016/j.cjche.2020.08.007
2. Aramrueang N, Asavasanti S, Khanunthong A. Leafy vegetables. In Z. Pan, R. Zhang & S. Zicari (Eds.), Integrated processing technologies for food and agricultural by-products. Cambridge: Academic Press; c2019. p. 245-272. http://dx.doi.org/10.1016/B978-0-12-814138-0.00010-1
3. Ara KM, Raofie F. Application of response surface methodology for the optimization of supercritical fluid extraction of essential oil from pomegranate (*Punica granatum* L.) peel. Journal of Food Science and

Technology. 2016;53(7):3113-3121. PMid:27765982. http://dx.doi.org/10.1007/s13197-016-2284-y
4. Mohamad N, Ramli N, Abd-Aziz S, Ibrahim MF. Comparison of hydro-distillation, hydro-distillation with enzyme assisted and supercritical fluid for the extraction of essential oil from pineapple peels. 3 Biotech. 2019;9(6):234. PMid:31139549. http://dx.doi.org/10.1007/s13205-019-1767-8
5. Hilali S, Fabiano-Tixier AS, Ruiz K, Hejjaj A, Ait Nouh F, Idlimam A, *et al.* Green extraction of essential oils, polyphenols, and pectins from orange peel employing solar energy: Toward a zero-waste biorefinery. ACS Sustainable Chemistry & Engineering. 2019;7(13):11815-11822. https://doi.org/10.1021/acssuschemeng.9b02281
6. Reis PMCL, Dariva C, Barroso Vieira GÂ, Hense H. Extraction and evaluation of the antioxidant potential of the extracts obtained from tamarind seeds (*Tamarindus indica*), sweet variety. Journal of Food Engineering. 2016;173:116-123. http://dx.doi.org/10.1016/j.jfoodeng.2015.11.001
7. Soquetta MB, Terra LDM, Bastos CP. Green technologies for the extraction of bioactive compounds in fruits and vegetables. CyTA-Journal of Food. 2018;16(1):400-412. https://doi.org/10.1080/19476337.2017.1411978
8. Safdar MN, Kausar T, Jabbar S, Mumtaz A, Ahad K, Saddozai AA. Extraction and quantification of polyphenols from kinnow (*Citrus reticulate* L.) peel using ultrasound and maceration techniques. Journal of Food and Drug Analysis. 2017;25(3):488-500. PMid:28911634. http://dx.doi.org/10.1016/j.jfda.2016.07.010
9. Daud MNH, Fatanah DN, Abdullah N, Ahmad R. Evaluation of antioxidant potential of *Artocarpus heterophyllus* L. J33 variety fruit waste from different extraction methods and identification of phenolic constituents by LCMS. Food chemistry. 2017;232:621-632. http://dx.doi.org/10.1016/j.foodchem.2017.04.018
10. Pal CBT, Jadeja GC. Microwave-assisted extraction for recovery of polyphenolic antioxidants from ripe mango (*Mangifera indica* L.) peel using lactic acid/sodium acetate deep eutectic mixtures. Food Science and Technology International. 2020;26(1):78-92. https://doi.org/10.1177/1082013219870010
11. Kupnik K, Leitgeb M, Primožič M, Postružnik V, Kotnik P, Kučuk N, *et al*. Supercritical fluid and conventional extractions of high value-added compounds from pomegranate peels waste: Production, quantification and antimicrobial activity of bioactive constituents. Plants. 2022;11(7):928. https://doi.org/10.3390/plants11070928
12. Júnior MES, Araujo MVR, Santana AA, Silva FLH, Maciel MIS. Ultrasound-assisted extraction of bioactive compounds from ciriguela (*Spondias purpurea* L.) peel: Optimization and comparison with conventional extraction and microwave. Arabian Journal of Chemistry. 2021;14(8):103260. https://doi.org/10.1016/j.arabjc.2021.103260
13. Selvamuthukumaran M, Shi J. Recent advances in extraction of antioxidants from plant by-products processing industries. Food Quality and Safety. 2017;1(1):61-81. https://doi.org/10.1093/fqs/fyx004
14. Sánchez-Camargo AP, Montero L, Mendiola JA, Herrero M, Ibáñez E. Novel extraction techniques for bioactive compounds from herbs and spices. Herbs, Spices and Medicinal Plants: Processing, Health Benefits and Safety, 2020, 95-128.
15. Sonar MP, Rathod VK. Microwave-assisted extraction (MAE) is used as a tool for rapid extraction of Marmelosin from *Aegle marmelos* and evaluations of total phenolic and flavonoids content, antioxidant and anti-inflammatory activity. Chemical Data Collections. 2020;30:100545. https://doi.org/10.1016/j.cdc.2020.100545
16. Sabrina Shen C, Eesha Khare, Nicolas Lee A, Michael Saad K, David Kaplan L, Markus Buehler J. Computational Design and Manufacturing of Sustainable Materials through First-Principles and Materiomics. Chemical Reviews. 2023 Jan 5;123(5):2242-75. https://doi.org/10.1021/acs.chemrev.2c00479
17. Sagar NA, Pareek S, Sharma S, Yahia EM, Lobo MG. Fruit and vegetable waste: Bioactive compounds, their extraction, and possible utilization. Comprehensive reviews in food science and food safety. 2018;17(3):512-531. https://doi.org/10.1111/1541-4337 .12330
18. Rudra SG, Nishad J, Jakhar N, Kaur C. Food industry waste: mine of nutraceuticals. Int. J. Sci. Environ. Technol. 2015;4(1):205-229.
19. Jiang T, Ghosh R, Charcosset C. Extraction, purification and applications of curcumin from plant materials: A comprehensive review. Trends in Food Science & Technology. 2021;112:419-430. https://doi.org/10.1016/j.tifs.2021.04.015
20. More PR, Jambrak AR, Arya SS. Green, environment-friendly and sustainable techniques for extraction of food bioactive compounds and waste valorization. Trends in Food Science & Technology; c2022. https://doi.org/10.1016/j.tifs.2022.08.016
21. Khaw KY, Parat MO, Shaw PN, Falconer JR. Solvent supercritical fluid technologies to extract bioactive compounds from natural sources: A review. Molecules. 2017 Jul 14;22(7):1186. https://doi.org/10.3390/molecules22071186
22. Uwineza PA, Waśkiewicz A. Recent advances in supercritical fluid extraction of natural bioactive compounds from natural plant materials. Molecules. 2020 Aug 24;25(17):3847. https://doi.org/10.3390/molecules25173847
23. Boyacı E, Rodríguez-Lafuente Á, Gorynski K, Mirnaghi F, Souza-Silva ÉA, Hein D, *et al.* Sample preparation with solid phase microextraction and exhaustive extraction approaches: Comparison for challenging cases. Analytica chimica acta. 2015;873:14-30. https://doi.org/10.1016/j.aca.2014.12.051
24. Patel AS, Kar A, Dash S, Dash SK. Supercritical fluid extraction of β-carotene from the ripe bitter melon pericarp. Scientific Reports. 2019;9(1):19266. https://doi.org/10.1038/s41598-019-55481-4
25. Farías-Campomanes AM, Rostagno MA, Meireles MAA. Production of polyphenol extracts from grape bagasse using supercritical fluids: Yield, extract composition and economic evaluation. The Journal of Supercritical Fluids. 2013;77:70-78. https://doi.org/10.1016/j.supflu.2013.02.006
26. Chavan P, Sharma P, Sharma SR, Mittal TC, Jaiswal AK. Application of high-intensity ultrasound to improve food

processing efficiency: A review. Foods. 2022;11(1):122. https://doi.org/10.3390/foods11010122
27. Sonawane A, Pathak S, Pradhan RC. Bioactive compounds in bael fruit pulp waste: ultrasound-assisted extraction, characterization, modeling, and optimization approaches. Biointerface Research in Applied Chemistry. 2020;11(1):9318-9334. https://doi.org/10.33263/BRIAC112.93189334
28. Montero-Calderon A, Cortes C, Zulueta A, Frigola A, Esteve MJ. Green solvents and Ultrasound-Assisted Extraction of bioactive orange (*Citrus sinensis*) peel compounds. Scientific reports. 2019;9(1):16120. https://doi.org/10.1038/s41598-019-52717-1
29. Kumar K, Srivastav S, Sharanagat VS. Ultrasound assisted extraction (UAE) of bioactive compounds from fruit and vegetable processing by-products: A review. Ultrasonics sonochemistry. 2021;70:105325. https://doi.org/10.1016/j.ultsonch.2020.105325
30. Gligor O, Mocan A, Moldovan C, Locatelli M, Crișan G, Ferreira IC. Enzyme-assisted extractions of polyphenols–A comprehensive review. Trends in Food Science & Technology. 2019;88:302-315. https://doi.org/10.1016/j.tifs.2019.03.029
31. Saad N, Louvet F, Tarrade S, Meudec E, Grenier K, Landolt C, *et al.* Enzyme-assisted extraction of bioactive compounds from raspberry (*Rubus idaeus* L.) pomace. Journal of food science. 2019;84(6):1371-1381. https://doi.org/10.1111/1750-3841.14625
32. Feng JY. In Study on the Bioactive Constituents of the Shell of Durio Zibethinus Murr. Guangdong: Guangdong Pharmaceutical University, 2017, 7–88.
33. Feng Jianying, Wang Yihai, Yi Xiaomin, Yang Weimin, He Xiangjiu. Phenolics from Durian exert pronounced no inhibitory and antioxidant activities. Journal of Agricultural and Food Chemistry. 2016;64(21):4273-4279.
34. Feng Jianying, Yi Xiaomin, Huang Wenjie, Wang Yihai, He Xiangjiu. Novel triterpenoids and glycosides from Durian exert pronounced anti-inflammatory activities. Food Chemistry. 2018;241:215-221.
35. Lameirão F, Pinto D, F Vieira E, F Peixoto A, Freire C, Sut S, *et al.* Green-sustainable recovery of phenolic and antioxidant compounds from industrial chestnut shells using ultrasound-assisted extraction: Optimization and evaluation of biological activities *in vitro*. Antioxidants. 2020 Mar 24;9(3):267. https://doi.org/10.3390/antiox9030267
36. Pelvan E, Olgun EÖ, Karadağ A, Alasalvar C. Phenolic profiles and antioxidant activity of Turkish Tombul hazelnut samples (natural, roasted, and roasted hazelnut skin). Food chemistry. 2018 Apr 1;244:102-8.
37. Riasari H, Fitriansyah SN, Hartati R, Anggadiredja K. Comparison of Extraction Methods, Antioxidant Activities, Total Phenol in Seeds and Seed Shells of Kabau (*Archidendron bubalinum* (Jack) IC Nielsen) From Lampung and South Sumatra. Pharmacognosy Journal. 2019;11(6).
38. Arumugam M, Manikandan DB, Sridhar A, Palaniyappan S, Jayaraman S, Ramasamy T. GC–MS-based metabolomics strategy for cost-effective valorization of agricultural waste: Groundnut shell extracts and their biological inhibitory potential. Waste and Biomass Valorization. 2022 Oct;13(10):4179-209.
39. Fernandez-Agullo A, Freire MS, Antorrena G, Pereira JA, Gonzalez-Alvarez J. Effect of the extraction technique and operational conditions on the recovery of bioactive compounds from chestnut (*Castanea sativa*) bur and shell. Separation Science and Technology. 2014 Jan 22;49(2):267-77.
40. Dashtdar M, Dashtdar MR, Dashtdar B, Khan SA. In-vitro, anti-bacterial activities of aqueous extracts of *Acacia catechu* (LF) Willd, *Castanea sativa*, *Ephedra sinica* stapf and Shilajit mumiyo against Gram-positive and Gram-negative bacteria. Journal of Pharmacopuncture. 2013 Jun;16(2):15-22.
41. Silva V, Falco V, Dias MI, Barros L, Silva A, Capita R, *et al.* Evaluation of the phenolic profile of Castanea sativa Mill. by-products and their antioxidant and antimicrobial activity against multiresistant bacteria. Antioxidants. 2020 Jan 20;9(1):87.
42. Cacciola NA, Squillaci G, D'Apolito M, Petillo O, Veraldi F, La Cara F, *et al*. *Castanea sativa* Mill. shells aqueous extract exhibits anticancer properties inducing cytotoxic and pro-apoptotic effects. Molecules. 2019 Sep 19;24(18):3401.
43. Lee CJ, Chen LG, Liang WL, Wang CC. Anti-inflammatory effects of *Punica granatum* Linne *in vitro* and *in vivo*. Food chemistry. 2010 Jan 15;118(2):315-22.
44. Lansky EP, Harrison G, Froom P, Jiang WG. Pomegranate (*Punica granatum*) pure chemicals show possible synergistic inhibition of human PC-3 prostate cancer cell invasion across Matrigel™. Investigational new drugs. 2005 Jan;23:121-2.
45. Malik A, Mukhtar H. Prostate cancer prevention through pomegranate fruit. Cell cycle (Georgetown, Tex.). 2006 Feb 15;5(4):371-3.
46. Lu QY, Arteaga JR, Zhang Q, Huerta S, Go VLW, Heber D. Inhibition of Prostate Cancer Cell Growth by an Avocado Extract: Role of Lipid-Soluble Bioactive Substances. J Nutr. Biochem. 2005;16(1):23–30. DOI: 10.1016/j.jnutbio.2004.08.003.
47. Butt AJ, Roberts CG, Seawright AA, Oelrichs PB, MacLeod JK, Liaw TY, *et al.* A novel plant toxin, persin, with *in vivo* activity in the mammary gland, induces Bim-dependent apoptosis in human breast cancer cells. Molecular cancer therapeutics. 2006 Sep 1;5(9):2300-2309. DOI: 10.1158/1535- 7163.MCT-06-0170.
48. Khalil EA. Antidiabetic effect of an aqueous extract of Pomegranate (*Punica granatum* L.) peels in normal and alloxan diabetic rats. The Egyptian Journal of Hospital Medicine. 2004 Jul 1;16(1):92-99.
49. Althunibat OY, Al-Mustafa AH, Tarawneh K, Khleifat KM, Ridzwan BH, Qaralleh HN. Protective role of *Punica granatum* L. peel extract against oxidative damage in experimental diabetic rats. Process Biochemistry. 2010 Apr 1;45(4):581-585.
50. Nogueira DG, Pereira NA. Effect of an extract of *Punica granatum* (pomegranate) in hyperglycemic mice treated with propranolol, Revista Brasileira de Farmacia. 1984;65(1-3):46-51.
51. Nozire O, Serpil D. Valuation of the pomegranate (*Punica granatum* L.) peels from the stand point of pharmacy, Ankara Üniversitesi Eczacılık Fakültesi Dergisi. 1993;22(1):121-122.
52. Alarcon-Aguilara FJ, Roman-Ramos R, Perez-Gutierrez S, Aguilar-Contreras A, Contreras-Weber CC, Flores-

Saenz JL. Study of the anti-hyperglycemic effect of plants used as antidiabetics. Journal of ethnopharmacology. 1998 Jun 1;61(2):101-110. DOI: 10.1016/ S0378-8741(98)00020-8.
53. Sathiyabama RG, Gandhi GR, Denadai M, Sridharan G, Jothi G, Sasikumar P, *et al.* Evidence of insulin-dependent signalling mechanisms produced by *Citrus sinensis* (L.) Osbeck fruit peel in an insulin-resistant diabetic animal model. Food and chemical toxicology. 2018 Jun 1;116:86-99.
54. Tsutsumi R, Yoshida T, Nii Y, Okahisa N, Iwata S, Tsukayama M, *et al.* Sudachitin, a polymethoxylated flavone, improves glucose and lipid metabolism by increasing mitochondrial biogenesis in skeletal muscle. Nutrition & Metabolism. 2014;11(1):32.
55. Fernando MR, Wickramasinghe SN, Thabrew MI, Ariyananda PL, Karunanayake EH. Effect of *Artocarpus heterophyllus* and *Asteracanthus longifolia* on glucose tolerance in normal human subjects and in maturity-onset diabetic patients. Journal of ethnopharmacology. 1991 Mar 1;31(3):277-282.
56. Marcillo-Parra V, Tupuna-Yerovi DS, González Z, Ruales J. Encapsulation of bioactive compounds from fruit and vegetable by-products for food application: A review. Trends in Food Science & Technology. 2021;116:11-23, https://doi.org/10.1016/j.tifs.2021.07.009
57. Lefebvre T, Destandau E, Lesellier E. Selective extraction of bioactive compounds from plants using recent extraction techniques: A review. Journal of Chromatography A. 2021, January; 1635:461770. https://doi.org/10.1016/j.chroma.2020.461770
58. Saavedra MJ, Aires A, Dias C, Almeida JA, De Vasconcelos MC, Santos P, *et al.* Evaluation of the potential of squash pumpkin by-products (seeds and shell) as sources of antioxidant and bioactive compounds. Journal of Food Science and Technology. 2015 Feb;52:1008-1015. https://doi.org/10.1007/s13197-013-1089-5
59. Vella FM, Laratta B, La Cara F, Morana A. Recovery of bioactive molecules from chestnut (*Castanea sativa* Mill.) by-products through extraction by different solvents. Natural Product Research. 2017, September 18;32(9):1022-1032.https://doi.org/10.1080/14786419.2017.1378199
60. Barbosa-Pereira L, Guglielmetti A, Zeppa G. Pulsed Electric Field Assisted Extraction of Bioactive Compounds from Cocoa Bean Shell and Coffee Silverskin. Food and Bioprocess Technology. 2018, January 13;11(4):818–835. https://doi.org/10.1007/s11947-017-2045-6
61. Sánchez-Camargo ADP, Ballesteros-Vivas D, Buelvas-Puello LM, Martinez-Correa HA, Parada-Alfonso F, Cifuentes A, *et al.* Microwave-assisted extraction of phenolic compounds with antioxidant and anti-proliferative activities from supercritical CO_2 pre-extracted mango peel as valorization strategy. LWT. 2021, February;137:110414. https://doi.org/10.1016/j.lwt.2020.110414
62. Gam DH, Hong JW, Kim JH, Kim JW. Skin-Whitening and Anti-Wrinkle Effects of Bioactive Compounds Isolated from Peanut Shell Using Ultrasound-Assisted Extraction. Molecules. 2021, February 25;26(5):1231. https://doi.org/10.3390/molecules26051231
63. Sharayei P, Azarpazhooh E, Zomorodi S, Ramaswamy HS. Ultrasound-assisted extraction of bioactive compounds from pomegranate (*Punica granatum* L.) peel. LWT. 2019, March;101:342-350. https://doi.org/10.1016/j.lwt.2018.11.031
64. Donatella P, Haraldsson M, Tagesson T. Do audit firm and audit costs/fees influence earnings management in Swedish municipalities?. International Review of Administrative Sciences. 2019 Dec;85(4):673-691.