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Utilization of citrus processing waste: A review

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Abstract
This review is strictly focusing on how remains or waste from citrus can be properly utilize rather than just discarding it. Citrus is one fruit that has been well known and is still known around the world for it enormous health promoting benefits and contains a huge quantities of by product that is a good sources of hemicellulose, essential oil, cellulose, and soluble sugars. When citrus remains or residue are properly utilize, it can be used as food for some animals and even be used as an organic matter in improving soil content. When citrus waste are properly utilize, it can serve as a potential and promising uses in places like food industry especially for the production of dietary fibre, pectin and as well in pharmaceuticals and cosmetic industries (flavouring agent, flavonoids extraction and citric acid) because there are high added value of compound that can be obtain or recovered from citrus processing waste with potential and Promising uses. Disposing of citrus processing waste may equally have a constraint both on environmental and economic factors because they may as well contains a higher level of essential oils and higher water content. Utilization of citrus processing waste can equally help to generate essential oil extraction, hydrogen syngas, production of bio-oil and charcoal etc. Through the adsorption technique, pulp produce from citrus is capable of serving as an effective agent for removing chemicals and metals in an effluent generated by-industries. However, proper utilization of citrus process waste may contribute to a potentially sustainable development and an unexploited resource (s). The utilization of citrus processing waste will be discussed in details below.

Keywords: Citrus, utilization, flavonoids, essential oils, hemicellulose, soluble sugars, flavouring agent

1. Introduction
Citrus processing waste play a strategic and monumental role in the field of agro-industrial areas, pharmaceuticals industries, cosmetic industries and animal feed industries. It can be harvested worldwide on a huge and large scale of land accounting for about 50-60% grand total of its production level and industrial importance (Satari and Karimi, 2018) [1]. Citrus processing waste production varies of about approximately 50% to 70% w/w of its fruits that has been processed depending on the technology that has been adopted and cultivars of fruit that is purposely based on the world annual production that is approximately around or closed to 10 million mg. The processing of citrus waste clearly validate a low pH and a higher concentration that is based on its organic compounds among which the availability of essential oils (EO, and that of which D-limonene being the primary constituent) is the key barrier for biological management options that is based upon their antimicrobial properties. A huge amount of citrus processing remains amounts a considerable constraints for their management due to both environmental and economic factors (Calabro *et al*., 2016) [2]. Citrus waste processing in which juice can also be formed is a vital rich source of vitamin C that is well and widely used for processing beverages that are so rich in nutrients. It also has a total of 50% of plain nice juice that is obtained and can be termed as a remains (seeds, pulp, and peel) and constitute a moisture capacity comprising of about 80% (Garcia-Castello *et al*., 2011; Rezzadori, Benedetti, and Amante, 2012) [3]. Such method that is used for waste management produces highly polluted waste water and may even lead to great degradation of the qualities of soil and causes huge damages to superficial waters in such areas (Braddock 1995; Martin, Siles, Chica, and Martin, 2010) [5, 6]. Waste from citrus are capable of containing essential oil which are made of compound like α-terpinolene, α-pinene, D-limonene, β-Citronellol, Citronellol etc. (Sahraoui, Vian, Maataoui, Boutekedjiret and Chemat, 2011) [7]. These essential oils that can be produce from citrus waste has wide range of application in cosmetic, pharmaceuticals and food industries as a flavoring agents in the preparation of cosmetics, soaps, food additives and beverages (Pereira, 2008; Raeissi, Diaz, Espinosa, Peters and Brignole 2008) [8, 9]. Of the above mentioned essential oil, D-limonene has the propensity to be

used as a safe and green solvent for the extraction of oil and replacing the toxic petroleum solvent like petroleum ether and as well be used as an effective solution for cleaning materials (Virot, Tomao, Ginies, Visinomi and Chemat, 2008) [10]. There are enormous fruit grown from citrus belonging to the family "Rutaceae". Processed citrus fruit waste comprises of high and beneficial phytochemical compounds (Yan *et al*., 2018) [91] that give out high demand in food, cosmetic and pharmaceuticals sectors. Citrus processing waste extracts are potential source of antibiotics that are found penicillin and metacillin that are used against pathogenic bacteria like salmonella typhi, bacillus subtilis, Escherichia coli, staphylococcus aureus and klebsiella pneumonia (Kumar *et al*., 2011) [38]. Proper utilization of citrus waste has helped in minimizing environmental problems and served as renewable means in recovering different bio-based products such as: bio-fuels, organic aids and enzymes (Nizami *et al*., 2017) [29]. When citrus processing waste has been used as bio-fertilizers, it serve as a rich source of phenols and carotenoids that helps improve and extend the shelf life of food and beverage (Okino Delgado and Flueri, 2016) [30]. Utilized citrus processing waste have been used in enzymes production particularly pectinase and xylanase that sum up a yield total of 265 U/g and 65 U/g from aspergillus niger through solid state fermentation process with a specific intensity of air flow of 1 V/kg M (Rodriguez-Frenandez *et al*., 2011) [34]. For the preparation of this review paper, I was able to use many search engines particularly PubMed, Google Scholar and Web of Science were consulted to retrieve the articles using the following key words: "citrus processing waste" "citrus" and "application of citrus waste".

This review paper mainly aim to encapsulate the recent studies on the application of citrus processing waste in food, cosmetic and pharmaceuticals sectors. Furthermore, the different kinds of bioactive compounds from citrus peel waste were also highlighted. The present paper therefore serve as a complete information pack about citrus fruits, its processing, type of wastes and their utilization to readers.

2. Citrus fruit: Types, composition and structure

2.1 Types of different citrus fruits grown

There are many types of different citrus fruit grown for which they belong to a specific family called "Rutaceae" and a subfamily called "Aurantioideae". Different citrus fruit grown also depends on their types and sizes. They have their own unique properties that that are helpful in various food industries and non-food industries too. Depending on their different types and sizes, they can be termed as limes, citrons, mandarins, grapefruits, pomelo and oranges (Garcia-Salas *et al*., 2013) [3]. Citrus are rich in pectin and consists of some secondary plant metabolites like: coumarins, carotenoids, flavonoids, alkaloids, essential oils, phenolic acids and limonoids that contains several bioactivities like: anti-cancer, anti-inflammatory, neuroprotective effects, anti-oxidative and cardiovascular protective effects that play a strategic role in health (Committee, 2010) [94]. A typical structure of citrus fruit is given in Fig. 1.

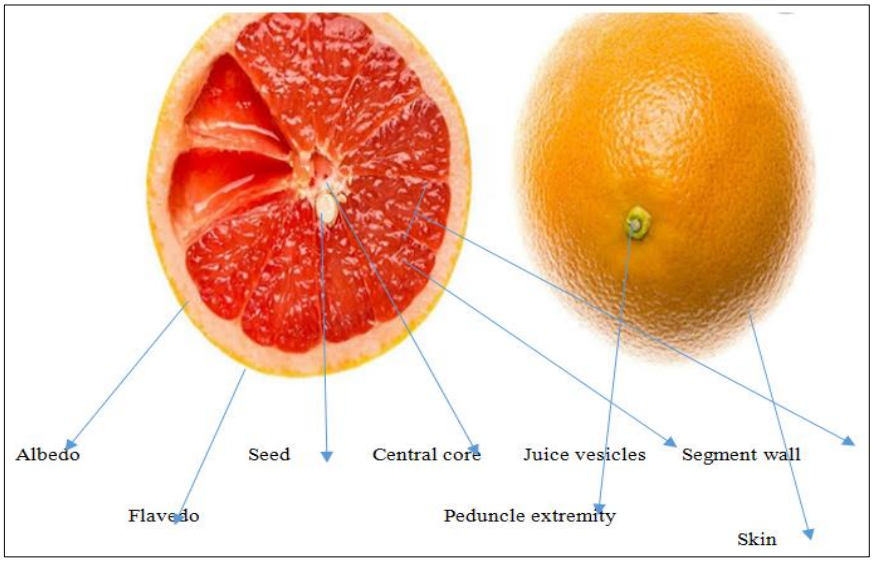

Fig 1: Structures of citrus fruit

2.1.1 Limes

Lime (*Citrus aurantifolia*) is associated with secondary plant metabolites like essential oils, carotenoids, alkaloids, phenolic acids and triterpenoids (Zhao *et al*., 2015) [11]. They became firstly well known in the Middle East and Asia. Limes is capable of curing liver diseases, heart diseases, bones and prevent urinary diseases. Limes can be cultivated worldwide under all inter-tropical, sub-tropical and mediterranean climates with about 15 Mt produced and serving as the third largest horticultural group for citrus (FAO, 2014) [95].

2.1.2 Citrons

Citrons (*Citrus medica*) is a fragrant fruit that has a thick large rind that can bear fruits almost as lemons but containing a less acid flesh. It has been formed to be an original aspect of the three fruits under citrus that was properly developed without synthetic hybridization or artificial hybridization. It can easily be described as a citrus with thicker peel than other citrus fruits. Citrons wild types were reported in Bhutan and Assam with it varieties being possibly acclimatized in Thailand, Yunnan and Vietnam (Froelicher *et al*., 2011) [96]. Citron has also been widely grown and distributed in Europe as an exotic and fashionable fruit (Brigand, 2010) [97].

2.1.3 Mandarins

Mandarins (*Citrus reticulate*) is a fruit that is highly

associated with important vitamins and minerals. Some of which can be properly utilized to form nice tasting juice with others being freshly consumed. Mandarin juices are pure, clear and sometimes cloudy. The production of mandarin has been ranked second after sweet orange contributing to 22% of citrus production worldwide (FAO 2016). Mandarin is a bit acidic and sweet in taste amongst the citrus family. The mandarin family were grown lastly in these various countries which are: India, Japan, East Indies and the southern part of China. Satsuma, tangerine and clementine are perfect examples of mandarin with high antioxidants and phenolic components being used as important ingredients in food and also being used for medicinal purposes (Zhang *et al*., 2014, Damian-Reyna *et al*., 2017) [98].

2.1.4 Grape fruits

Grapefruits (*Citrus paradisi*) is a subtropical fruit that is less sweet in taste, and large in size. Oils that are extracted from grapefruits particularly from it seeds can be processed and be used in sweet smelling agents like fragrance, soap and cosmetics (Flamini and Cioni, 2010) [100]. Essential oils extracted from grapefruit is known to be a good source of bioactivities that helps induce the growth of pathogenic strains and bacteria responsible for food spoilage (Uysal *et al*., 2011) [101]. Grapefruits extracts containing non-volatile phytochemicals and mixture of other essential oils can as well stops the proliferation and growth of cancer cells like: Leukemias, lungs and prostate cancer and neuroblastoma (Diab, 2016) [102].

2.1.5 Pomelo

Pomelo (*Citrus maxima*) is similar to grapefruits especially in the aspect of its natural taste and its flavour. Pulp from pomelo are known to be bitter. Amongst the citrus family "Rutaceae", crop grown by pomelo ought to be the largest crop. Pomelo can be used as a medicine to prevent peroxidation damage, cardiovascular diseases, lack of vitality, hyperlipemia, acne, wounds or osteoarthritis (Aumeeruddy-Elalfi *et al*., 2016) [103]. Pomelo constitute minerals, water and vitamin that serve as an active physiological ingredients like: volatile oil, flavonoid, limonoid and coumarin (Zhang *et al*., 2011, Tsai *et al*., 2017) [47, 104].

2.1.6 Orange

Orange (*Citrus sinesis*) has a pulpy carpels and appears round in shape. It can be used in industries for producing sweet beverages that contains citrus. It has two varieties namely horned orange and bitter orange. When is has turned ripe, it becomes easily distinguishable and separable with it reddish yellow color. Orange became well known in Southern China, Northeast India and Myanmar. Orange serve as a good source of pectins, vitamin C, phenolic compound and flavonoids. Flavonoids that are found mostly and easily seen in orange are: naringin, hesperidine, eriocitrin and narirutin (Gaurnieri *et al*., 2007, Kamran *et al*., 2009) [106, 107].

2.2 Bioactive and nutritional composition

Waste that are obtain from citrus has a higher sugar level that is necessary for fermentation in bioethanol production (Choi *et al*., 2013) [12] and as a substrate for fermentation through a solid state (Couto and Sanroman., 2006) [13]. Waste that are discarded from citrus like peel, seeds, juice vesicles and membrane contribute enormously to an economic valuable source of high- added valuable compounds that may contains efficient amount of dietary fibre, flavonoids, polyphenols, sugars, carotenoids, ascorbic acids and essentials oils, as discussed in Table 1.

Table 1: Summary of bioactive components derived from citrus processing waste

Bioactive compound(S)	Benefits	Citrus based sources	Reference
Dietary fibre	Serves as an integral source in human diet by reducing the risk of many diseases like cardiovascular and diabetic diseases. Help in weight loss, reduce hypertension attack and prevent coronary heart disease.	Pulp and peel	Anderson *et al*., 2009 [111] Birketvedt *et al*., 2005 [112] Whelton *et al*., 2005 [113] McRae 2017 [114] Mahato *et al*., 2019 [115]
Phenolics	It can be used for medicinal and traditional purposes. It acts as a powerful antioxidant that prevents cells from high risk of cancer, prevent tumour and prevent free radicals damages.	Peel and pulp	Singh *et al*., 2018 [116]
Essential oils	Serves as a commercial antimicrobial agent in preventing food deterioration and food contamination. It contains antifungal, insecticidal and antibacterial properties to help preserve food and extend it shelf life.	Peel	Gormez *et al*., 2016 [117] Pandey *et al*., 2017 [118]
Carotenoids	Carotenoids are essential in animal feed additives, neutraceuticals and pharmaceuticals areas and also acts as a colouring agent in foods and cosmetics products.	Peel and pulp	Das *et al*., 2007 [119] Mortensen, 2009 [120]
Pectin	Benefits of pectin in food is that it can be used as stabilizer and gelling agent in food. Helps to stops or prevent poisoning and cure diabetes and gastro oesophageal reflux disease.	Peel	Kanmani *et al*., 2014 [121]

Table 2: Summary of application of citrus by product bioactive compounds in food processing, pharmaceutical and cosmetic industries

S. No.	Product name or brand name	Manufacturer	Bioactive compound used/added	Purpose	Reference
Food applications					
1	Biscuit (Parle g)	Parle Products	Phenol, terpenoids and flavonoids	To enhance the colour, functional properties, antioxidant activity and to make product hard.	Manjiote *et al*., 2017
2	Chips (Lays)	PepsiCo	Phenolics, dietary fibre, potassium and ascorbic acid	To protect health against oxidative damage and restrict degenerative diseases associated with oxidative stress	Al-Weshahy *et al*., 2010 [78]

3	Cakes (Groundnut)	Indmak corporation	Flavonoids, phytosterols, phenolic acids, resveratrol and arginine	To reduce blood pressure, reduce inflammation, expand blood vessels, reduce cholesterol, prevent platelet from the arteries and improve longevity	Craft *et al*., 2010 [79]
4	Drinks (Coca-Cola)	Coca-Cola company	Theobromine, caffeine and flavonoids	Aid in urination, acts as a heart stimulant and increase insulin resistance.	Katz *et al*., 2011 [80]
Pharmaceutical applications					
S. No.	**Product name or brand name**	**Manufacturer**	**Bioactive compound used/added**	**Purpose**	**Reference**
1	Oral drugs (Amoxicillin)	Medicef	Antibiotics	Helps to treat bacterial infections in throat, nose, lungs, urinary tract, skin and ear.	Michelle Llamas, 2021
2	Oral drugs (Paracetamol)	Sri Krishna Pharmaceuticals	Zanthoxylum armatum, steroids, flavonoids	Stops pains, inflammation, induced hepatotoxicity in rats and inhibits oxidative stress	Veda priya *et al*., 2017 [81]
Applications in cosmetic industries					
S. No.	**Product name or brand name**	**Manufacturer**	**Bioactive compound used/added**	**Purpose**	**Reference**
1	Cream	NutriGlow cosmetics pvt. Ltd	Flavonoid (spinacetin, quercetin, vanillin, patuletin and ferulic acid)	Because it contains anti-aging properties, decreases number of senescence cells in normal fibroblast and protect human fibroblast cells from senescence and reduce inflammation.	Ahlina *et al*., 2020 [84]
2	Perfume	Keva perfume and fragrances	Terpenoids (citronellal, nerol, citronellol and linalool	Terpenoids are used in cosmetic because it helps improve the aroma and flavour of the products.	Sell, 2006 [85] Pavela, 2015 [86]

2.2.1 Dietary fibre

Dietary fibre that is present in citrus fruits are divided into two types which are the soluble fractions and the insoluble fractions. Those one that are term as soluble fibre are: gum and pectin while the insoluble are: lignin, cellulose and hemicellulose. Citrus fibre can be considered as a blood alcohol content (BAC) because of it availability in adding polysaccharides from polyphenolic components that can be strongly used as potential inhibitor for oxidizing products containing lipids like meat and at the same time improving the total oxidative stability and extending the shelf life of meat products (Fernandez-Gines *et al*., 2003, Sayago-Ayerdi *et al*., 2009) [15, 16]. Orange juice fibre (seeds, pulp and peel) have been used as a novel replacer for fat in ice cream due to its oil and water retention capabilities (de Moraes Crizel *et al*., 2013) [13]. They are easily known as polysaccharides (non-starch) with more than ten or ten units of carbohydrates that are not easily broken down or digested within the smaller intestine of humans.

2.2.2 Phenolics

Citrus peel contains rich natural flavonoids in higher amounts. Some of those flavonoids includes: anthocyanidins, flavonols, flavanones, isoflavanones and flavanols. There are other small phenolic acids found in citrus peel like *p*-coumaric, chlorogenic, sinapic, caffeic and ferulic that can be found in the waste of citrus (peel) comprising of neo-hesperidin, naringin and neo-eriocitrin serving as the key flavanones available in the waste of lemon, orange and bergamote with a statistics indicating 400-600 mg/100 g in lemon peel, 380-1100 mg/100 g in sour orange peel and 400-1000 mg/100 g in bergmote peel (Bocco *et al*., 1998, Mandalari *et al*., 2006) [18, 19]. Those polyphenolic compounds give rise to the numerous and high antioxidant activities of citrus and make it more versatile because they are not only used in food products but in beverage, cosmetic and pharmaceuticals industries. Citrus by-products are also known for having a higher level of scavenging properties for inhibiting free radicals activity and can be arranged into two sub-groups which are: hydrocinnamic acids (p-coumaric, ferulic, sinapic and caffeic acids) and hydroxybenzoic (syringic, gallic and vanillic acids) (Ignat *et al*., 2011) [22]. Citrus by-products or waste has more or higher amount of polyphenols more that even the part that can be consume or edible. In the citrus family, lemon waste tend to contain acceptable amount of chlorogenic acid, gallic acid, ferulic acis, naringenin and rutin while it seeds tend to have eriocitrin and caffeic acids (Xi *et al*., 2017).

2.2.3 Availability of EOs (Essential oils)

It is true that essential oils found in citrus waste (peel) are frequently used in some pharmaceuticals, food and cosmetic industries because they have the propensity to act as a flavouring agent and give out sweet smell (fragrance) in food, beverage and pharmaceuticals products and has been used since ancient times. Essential oils comprises of some monumental constituents that give rise to its make up and those constituents include: alkenes, acids, alcohol, aldehyde, phenols, ketones, nitrogenated compounds and esters (Oprean *et al*., 1998) [20]. Essential oils being an aromatic and volatile compounds, it also has some health benefits attached to it like anti-inflammatory properties, antifungal, antibacterial, insecticidal and anti-viral properties. Essential oils are lipophilic molecules with low aqueous solubility (Thormar H. 2011) [21]. Due the high level of antioxidants, biological and antimicrobial properties of essential oils that are produced from citrus waste, it was given the GRAS (Generally Recognized as Safe) status by the Food and Drug Administration (FDA). It also obtained the GRAS status because of it can equally be used as a flavoring agents in pharmaceuticals, cosmetic, aroma-therapeutic properties and food industries (Satari B and Karimi K, 2018) [1] Composition of chemicals from essential oils and it yields is based particularly on method used for its oil extraction. Monoterpenes and sesquiterpenes are compounds from two and three isoprene units that generally make up the structure of essential oils. In essential oil, monoterpene are monumental because they are available for the extraction process particularly in plants that have vegetables, herbs, spices and fruits. Monoterpenes is responsible for the falvor and aroma of plant from which it has been extracted from. It

consist of an anti-carcinogenic activities that actively works at different levels (cellular and molecular). Meanwhile, monoterpenes which are compounds that function highly as an anti-tumorigenic and as a non-toxic agents can also acts as an anti-cancer medicine in animals. Sesquiterpenes as a three isoprene unit compound found in citrus waste and other plants can prevents toxins and growth of microbes from damaging the immune system due to its antioxidants ability to build and repair cells. Sesquiterpenes that are present in essential oils, helps extremely in preventing the brain against the growth of tumor, un-wanted cellular growth and aids in neurological health. Sesquiterpenes are also known to cure skin diseases, improve growth and build the white blood cells and the respiratory systems (Saratoga 2020). Below are Fig. 2 and 3 showing the chemical representation of sesquiterpenes and monoterpenes.

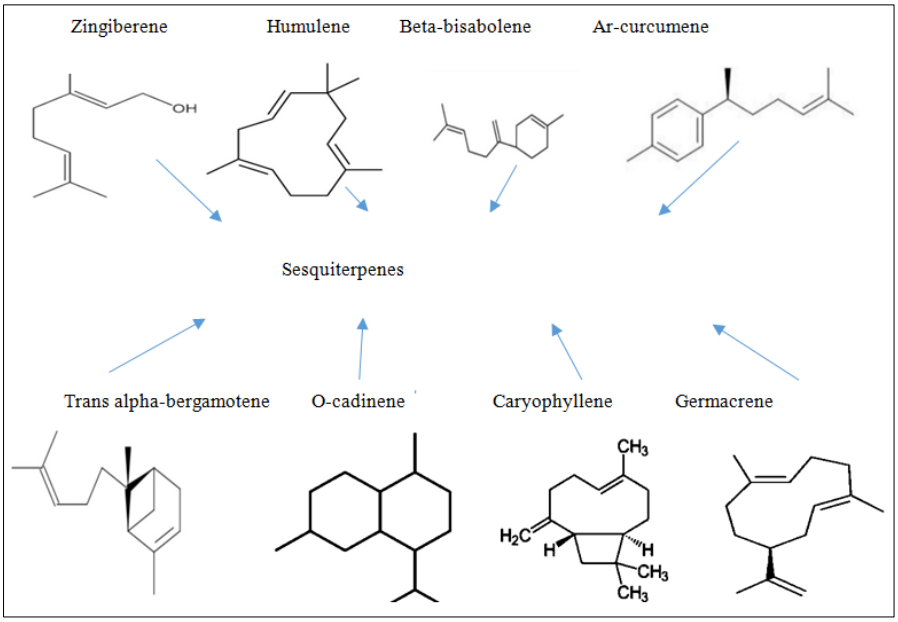

Fig 2: Chemical representation of sesquiterpenes

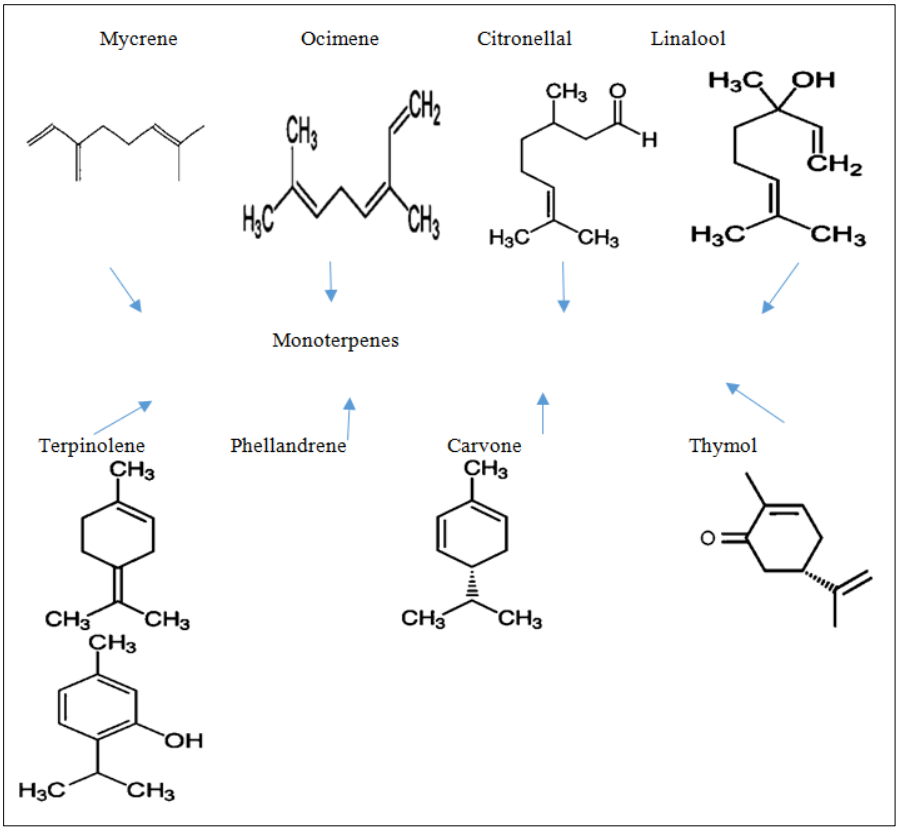

Fig 3: Chemical representation of monoterpenes

2.2.4 Carotenoids

Carotenoid is colour change pigment found in plants and found also found in raw materials and biological properties. Pharmaceuticals and cosmetic industries rely seriously on carotenoids for its chemical synthesis and industrial production. Carotenoids are applicable in the fortification of food due to their potent activities needed for strengthening the body's immune system and reducing degenerative

diseases risk (Niizu., 2016) [26]. Several types of carotenoids are discussed in Fig. 4. Carotenoids has vitamin A that is also monumental in building up the epithelial tissues, providing proper growth, strengthening the white and red blood cells in the immune system, revamping of photoreceptors and tissues and promoting visual cycle (C.L.B. Ambrosio *et al*., 2016) [27]. There are two main types of carotenoids that are mainly found in citrus waste and that which include the hydrocarbon carotenoids and the oxygenated carotenoids. The hydrocarbon carotenoids is further divided into subgroups like lycopene and beta carotene while the oxygenated carotenoid can be further divided into xanthophylls, violaxanthin and lutein (Saini, R.K and Keum Y.S, 2018) [25]. Zexanthin and Lutein there are two polar pigments that collectively in carotenoid at a higher level and they can be present in spinach, egg yolk, and as well food containing lutein (Snodderly D.M., 2013) [28].

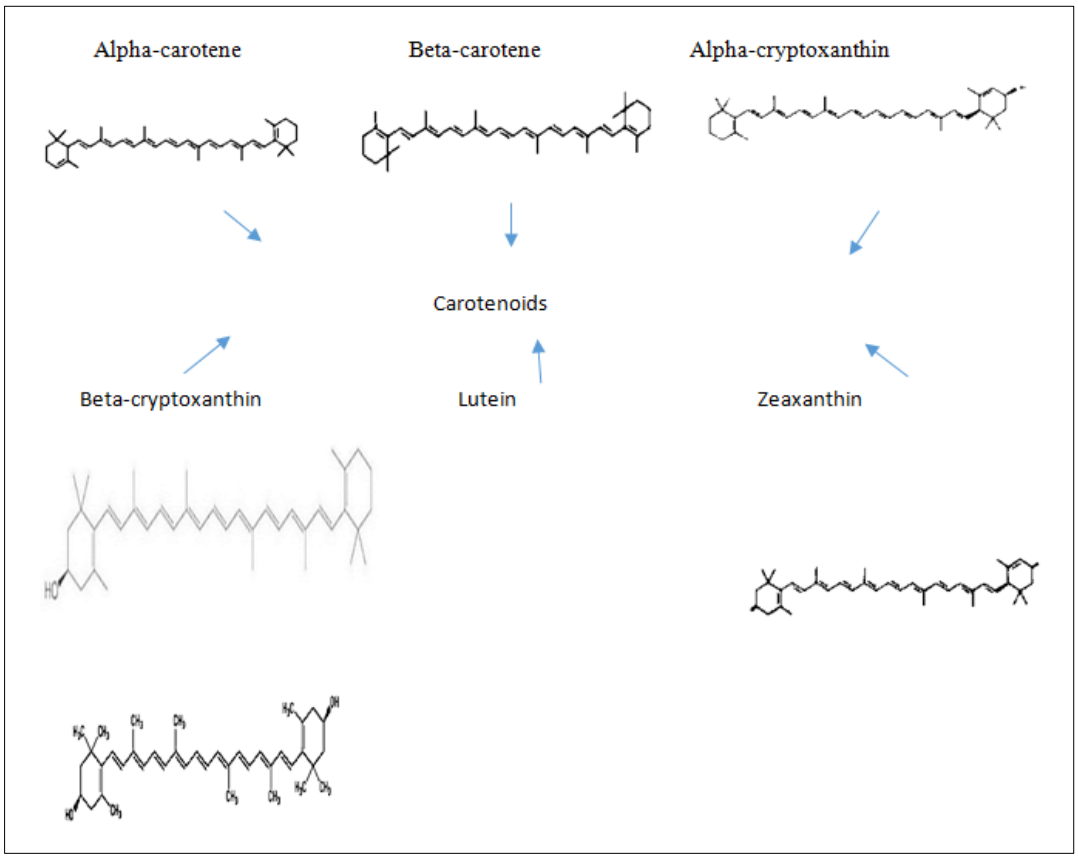

Fig 4: Chemical representation of carotenoids

2.2.5 Pectin

Pectin is a polysaccharides that is mostly found in fruits and vegetables that can act as an ingredients jams, jelly and marmalade. When a water concentration gets low, pectin can behave as a hydrocolloid which is then able of trapping forming gels and water. This process is done because pectin has a thickening agent and stabilizing properties that is applicable in the production of sweet foods. Pectin usually consists of four types of polysaccharides that contribute to its makeup namely: Rhamnogalacturonan type I (RGI), rhamnogalacturonan type II (RG-II), xylogalacturonan and homogalacturonan with the most abundant being known as RG-I and HG (Karboune and Khodaei, 2016) [39]. Due to it solubility in water, it can widely be used as desirable texture in water. However, due to its biocompatibility, chemical versatility, edibility and biodegradability, pectin can acts as a strong matrix in the production of active edible films with huge applications in the packaging and safety of food (Espitia *et al*., 2014) [40]. Pectin has a versatile and diverse nature most especially when it has been extracted or removed from citrus. Pectin has been used in food products as a texturizing, thickening, emulsifying and stabilizing properties in bakery products, jams, biodegradable products, jellies and as well as confectionary products (Espitia *et al*., 2014) [40].

3. Citrus processing waste: An overview

The processing and managing of citrus waste should be given an increase attention because waste obtained from citrus constitute high level of vitamin C, can be used in juice making and producing beverages with rich nutrients. The seeds, pulp and peel which are considered as remains or residues are disposed in water, land or even burned in the process causes environmental problems like water contamination, depletion of oxygen and pollution of environment (Wadhwa and Bakshi, 2013) [4]. Citrus by products are discussed in Fig. 5.

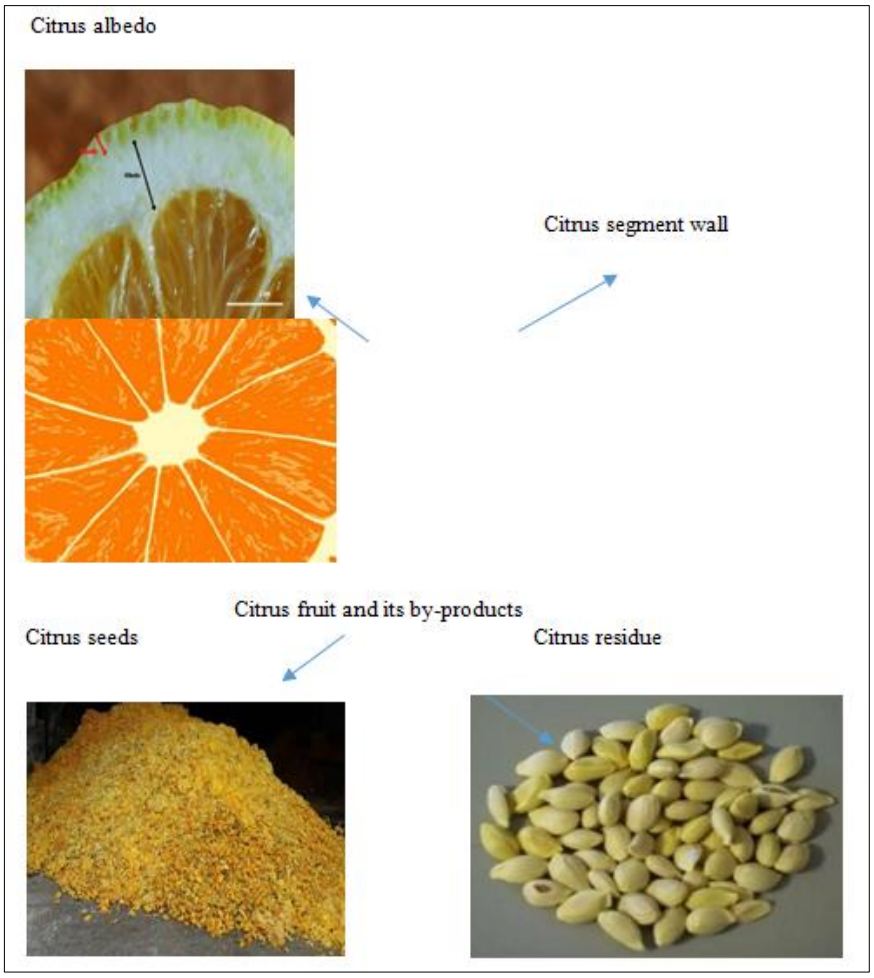

Fig 5: Pictorial view of citrus fruits and its by-products

Proper processing and managing of citrus waste can be used to produce bio-oils, ethanol, essential oil and organic fertilizers which may help generate profits for industry and prevent environmental problems. Citrus waste are good source of soluble pectin (42.5 g/100 g), being the most monumental component hemicelluloses (10.5 g/100 g), cellulose (9.21 g/100 g) and sugar (16.9 g/100 g) which indicates that citrus waste especially when it has been processed are highly rich in insoluble and soluble carbohydrates with huge valuable products through subsequent chemical and biological processes (Rivas *et al*., 2008) [87]. Pectin that are found in citrus processing waste and other green fruits and vegetables are multifunctional polysaccharides are widely applicable in food industry as a thickener, emulsifier, stabilizer and gelling agent. Due to its diverse and versatile chemical structure that is capable of interacting with number of various molecules to establish novel materials with promising utilization in pharmaceuticals areas and control the delivery of drugs especially for targeted colon ones that has the ability prevent acidic conditions, treatment and health care (Bonaccorsi *et al*., 2011) [88]. Citrus processing waste play a very monumental role in biosorbent and also a good source for lignocellulosic biomass because waste obtained from citrus processing has a low lignin content and rich in carbohydrate. Lignocellulosic biomass obtained from the waste of citrus is efficient in removing low concentration contamination, cost effective, simple design, rate of high adsorption and gives out small by-product at the end of adsorption (Marina and Gadd, 2014) [89]. Lignocellulosic biomass gathered from citrus waste can be used for removing Pb2 +, Co2 + and heavy metal from an aqueous solution depending on the size of particle containing a bio-sorbent material, the solution's pH, speed at which it has shaken during an experiment, solution's temperature, concentration of initial metal ions, employed bio-sorbent dosage and contact time between bio-sorbent and the test media (Bhatti *et al*., 2010) [90]. Citrus processed waste constitute of high and beneficial phytochemical compounds (Yan *et al*., 2018) [91] that promote high market demand for its use in pharmaceuticals, food and cosmetic industries. Flavonoids, polysaccharides, oligosaccharide, pectin, essential oils and terpenes are important compounds founds in citrus processing waste to help promote and increase it cost and value (Zema *et al*., 2018) [92].

4. Application of citrus processing waste

4.1 Application of citrus utilization waste in pharmaceuticals industries

Citrus seeds contains oil that is applicable in the production of ear drops, disinfecting and sterilizing agents, nasal drops for infections and cold, nebulizers for controlling respiratory diseases and infections, ointments, pesticides, medicines and throat gargles. Extracts that are produce from it peels contains saponins, flavonoids and alkaloids that has anti-typhoid activities that can be used against salmonella typhi A in higher amount and against salmonella typhi in smaller amount (Kumar *et al*., 2010) [36]. Oil produce from bergamot has anti-inflammatory activity that is applicable in pharmaceuticals to produce drugs that will be able to induce

hepatotoxicity and oedema in rats and possess lots of promising effect (Mehmet *et al*., 2010) [37]. Extracts from citrus limon and citrus sinesis are potential antibiotics that can be found in the production of penicillin and metacillin that are used against pathogenic bacteria like bacillus subtilis, salmonelly typhi, staphylococcus aureus, klebsiella pneumonia and Escherichia coli (Kumar *et al*., 2011) [38]. Utilizing citrus waste in pharmaceuticals is necessary because of it antioxidants activity that helps in inducing enzymes and inhibiting expression of gene. The natural antioxidants activity of citrus is highly linked with therapeutic activities like: antimicrobial, cardioprotective, antiallergenic, anti-inflammatory, antithrombotic and antiatherogenic effects that makes it a good source of bioactive compounds (Castro-Vazquez *et al*., 2016, Shirahigue and Ceccato-Antonini., 2020) [46, 83].

4.1.1 Flavonoids

Flavonoids play a vital role in pharmaceuticals industry because when it has been taken on a daily basis, it helps minimizes the risk of higher chronic diseases that involves neurodegenerative disorders, cancer and cardiovascular disease. There are many types of flavonoids that play different pharmacological roles like rutin and quercetin that consist of high inflammatory properties and another being known as neohesperidin and hesperidin which are all flavonones that helps stops and prevent the damaging of DNA and as well prevent hydrogen peroxide toxicity (Simmonds., 2003 and Simmonds and Stevenson., 2001) [41, 42]. Flavonoids possess an antioxidant activity that helps in lowering high level of cancer, scavenging free radicals, respiratory disorder, early ageing and serve as an important constituent in lowering oxidative stress due to it versatile health benefits and physiological potent activities as a secondary plant metabolites (Falcone *et al*., 2012) [43]. There are two most powerful flavonoids (catechins and flavones) that play an enormously role in preventing the body against reactive oxygen species (ROS) and contribute to it pharmological properties like: anti-microbial activity, antioxidant activity, anti-inflammatory activity, anti-fungal activity, anti-diabetic activity, anti-viral activity, vasorelaxant agent, anti-ulcer activity, antiatherosclerotic effects, hepatoprotective activity, cardio-protective effect, anti-thrombogenic effects, antineoplastic activity and effect on central nervous system. Flavonoids serve as a key factor in the above mentioned health factor the helps in promoting a better health and wellbeing and due to it all important health benefits, pharmaceuticals industries decides on using it in their health related products. Flavonoids are applicable in pharmaceuticals because they have solubility in water that equates them as potent candidates in the production of drugs (Aglycones). Secondly, flavonoids has a shorter duration of time within the small intestine with a low rate of absorption thus preventing the body against toxic effects of consuming flavonoids rich food (Asha *et al*., 2014) [71]. Flavonoids as a secondary plant metabolite, it helps lowers the levels of lipids cholesterol of blood and as well stops the role of antimicrobial against microorganism "Staphylococcus aureus" (Lee *et al*., 2013) [72].

4.1.2 Carotenoid

Carotenoids are essential in pharmaceuticals industries because it can be processed as a nutraceutical food as a means of minimizing chronic diseases and acting as a bioactive compounds in improving health. Carotenoids can act a powerful antioxidants and prevent cells against singlet oxygen that is formed in the tissues and against free radicals (Jomova and Valko. 2013) [44]. Carotenoid contains vitamin A, cryptoxanthin, α-carotene and as well as β-carotene that serve as a potential source of biological maintenance that constitute immunity and reproduction. Beta carotene found in carotenoids can be available in tissues and blood that is highly linked with antioxidant activity that helps built up cell and improve metabolism against free radicals and reduces higher doses of health risk (Curhan *et al*., 2015) [45]. Neochloris oleoabundans carotenoids can induce the growth of colon cancer cells with astaxanthin, beta-carotene and capsanthin having an antiproliferative effect against leukemic K562 cells (Zhang *et al*., 2011 and Castro-Puyana *et al*., 2016) [46, 47].

4.1.3 Limonoids

Limonoids are secondary plant metabolite that can be found in citrus fruits with lots of promising health benefits. They have the propensity to help in serving as an antiviral agents, anticancer agent, insecticidal activity, hypocholesterolemic activity, as well as reducing cholesterol level. Pharmaceuticals industries consider using limonoids due to those potential health benefits it possess. Citrus limonoids contains anticancer bioassays activities that has been proved that two limonoids obacunone and limonin can be used to prevent or stops azomethane (AOM) and as well inhibits the growth and development of colon tumorgenesis the was evaluated in rats (Tanaka *et al*., 2000) [48]. Limonoid glucosides and deacetylnomilin have found to be those two effective limonoids that helps strategically in inhibiting the negative cells growth of estrogen receptors. Nomilin was observed to be the efficient and effective limonoid in inhibiting the estrogen receptorpositive breast cancer cells while limonoid analogue being synthetic and was also observed to be the potential inhibitor in inhibiting the estrogen negative cells (Hasegawa *et al*., 1980) [49].

Limonoids (Triterpenoids) which are phytochemicals formed from limonin are applicable in pharmaceutical industry because they possess a wide range of biological activities like antibacterial, anticancer, antimalarial, insect antifeedant, insecticidal, antiviral anti-inflammatory and antifungal activities that have pharmacological importance in human (Roy and Saraf., 2006) [73].

4.1.4 Beta carotene

Beta carotene is a carotenoid that is formed part of the provitamins groups which is highly related with Vitamin A. It is a pigment that is formed part of plant that is associated with colors like yellow, orange and red in vegetables and fruit. Pharmaceuticals industries allows beta carotene in their products because it can acts as a supplements for nutrition, colorants, and antioxidants as well as dietary supplements. Beta carotene is used in pharmaceuticals industry because it has the propensity to stops or inhibits arthritis, specific cancers, lowers heart diseases of high risk and stops skin diseases and asthma. It can also act as a nutrient supplement and vitamin A source for infant. It acts as an agent in minimizing the activity of photosensitivity in sick person with photosensitivity diseases and erythropoietic protoporphyria (Matthew-Roth *et al*., 1977) [50]. Beta carotene used in pharmaceuticals industries can help to enhance the resistance to inflammation, improve the

production of RNA, boost immune response due to its detoxifying properties, lowers the growth of apoptosis, lowers oxidative stress and promotes antioxidants activity (Ramachandrayya *et al*., 2015) [51].

4.1.5 Dietary fibre
Dietary fibre is a plant produced food that is not easily digested or synthesize by the body. However, absorbing food without or less number of dietary fibre may cause or lead to diseases like obesity, gallstones, constipation, coronary heart diseases, and diabetes as well (Sudha *et al*., 2011) [52]. On the basis of such, pharmaceuticals industries tends to apply dietary fibre in their products due to its high beneficial health properties that it exhibits. The increase consumption of dietary fibre slower downs the risk of stroke development and colorectal cancer (Zhang *et al*., 2013 and Dahm *et al*., 2010) [53, 54]. Proper intake of dietary fibre slower down overweight in adults, toddlers and lowers serum cholesterol as well as high blood pressure (Brown *et al*., 1999 and Quick *et al*., 2013) [55, 56].

4.1.6 Folic acid
Folic acid is a vitamin found part of the B complex group that can be available in avocado, kidney, liver, vegetables and some fruits as well. Folic acids comprises of so many health promoting benefits that seeks pharmaceuticals industries interest. Folic acid is used in pharmaceuticals industries because it is certainly vital in the separation of rapid cells like erythropoiesis, pregnancy infancy, and prevent cancer development. Another pharmaceuticals aspect about folic acids is that it acts as an important cofactor specifically for enzymes that require the synthesis of RNA and DNA. Folic acids is needed by the body in order to break down or synthesis methionine, pyrimidines and purines before applying such into a protein or DNA. Folic acids only works effectively and efficiently within the body when it has been firstly broken down or reduced with the presence of dihydrofolate reductase (DHFR) and then transferred into tetrahydrofolate (THF) and dihydrofolate (DHF) which served as a cofactors in order to give rise to amino acids and nucleic acids within the body (Salbaum and Kappen., 2012) [57].

4.2 Application of citrus utilization waste in food industries
Utilizing citrus waste in food industries is important and an ideal means of improving food product and health. It helps in the make-up of high quality rich food and nutritious rich beverages. In food industries, those wastes obtained from citrus are used for producing animal feed, producing pectin, serving as an encapsulating agent, producing Kraft paper for food and developing of bio-degradable packaging. Organic acids obtained from citrus waste can also be used as a functional constituents for the processing of food. It helps in improving the aroma of the food, improving it taste and quality, curing deficiencies, serving as a supplement for nutrients, better preservatives and improving flavour in food due to its antioxidants (Kaur and Kapoor., 2001) [58].

4.2.1 Alkaloids
Alkaloids are used in food industries because many of it can be an element in diet in humans. They can be found in the seeds of cacao, leaves of tea, cocoa seeds, potatoes and tomatoes. Alkaloids are present in beverage products and helps enhance drinks taste especially in coca-cola. It presence in beverages helps to stimulate a person who is actively involved in sporting activities and consuming drinks containing alkaloids (caffeine) (Joanna Kurek., 2019) [59]. Alkaloids are used in other food products because they possess a potential bioactivities like atropine and caffeine (Joanna Kurek., 2019) [59].

4.2.2 Nitrogenous compounds
Nitrogenous compounds are those compounds that originates from ammonia, nitric acid, cyanogen and hydrogen cyanide. They are known to be related ammonia because of its relationship amides, and amino acids. Nitrogenous compound are used in food industries because they are capable of transforming reactive nitrogen forms of mineral (Nr) like ammonium and nitrate into nitrogenous organic compound like nucleotides and amino acids that serves as a main constituents for nucleic acids and proteins which are beneficial for life. The presence of these main forms of minerals Nr are important sources in determining the yield of crops for food, bio-energy, fibre and feed for the benefits of human activities (Sutton *et al*., 2011) [60]. Food industry also use nitrogenous compound because it helps to extend the shelf life of food and minimize the chances of food oxidizing and turning rancid or stale.

4.2.3 Carotenoids
Naturally carotenoids are pigments form from plant that are responsible for colour change. Carotenoids are used in food industries due to its ability to acts as a colorants in many drinks and food products. Due to the high amount of antioxidants in carotenoids, it can be used in the fortifying of food and supplementation. Carotenoids can acts as an encapsulating agent in encapsulating the functional lipophilic components such as: bioactive lipids and flavors with the presence of beta carotene. Beta carotene has been known as the most important member of within the carotenoids family because it can act as a precursor for retinol with high rate of conversion. Carotenoids provides higher amount of vitamin A in human diet and act as functional ingredients in food (Naves and Moreno 1998) [61]. These colourful pigments are used as colorants for food such as: meat, red soy cheese, by-products of fish and meat and wine (Dufosse *et al*., 2005) [74]. Carotenoids can add or improve the color, flavour, and aroma of food due to its antioxidants properties it possess. They are also available in French cheese because of its brown-orange-red colour that helps enhances the sensory quality of food product (Galaup *et al*., 2015) [75].

4.2.4 Polyphenolics
Polyphenolics are those compounds from secondary plants metabolites that are extracted from natural sources like vegetables, grapes, spices, rice, tea and algae, herbs and olives. They are used in food industry because they improve the functionality of food and extends its shelf life. Polyphenolics in food helps preserves foods that are perishable through many process like oxidation processes or microbial spoilage. It enhance the value of food through fatty acids or vitamins, minerals and protein. It prevent odors and off-flavors from food leaving free from foodborne diseases that might cause food to be unsafe for consumption. Polyphenolic compounds used in food industry helps stops the deterioration of food due to it biopreservatives.

Biological activities from polyphenolics compounds allows food to be produced without the presence of chemical addicitves. Polyphenolics in food industry prevents the degradation of endogenous antioxidants (Penalvo *et al*., 2016) [62]. Polyphenolics also prevents the production of harmful glycation in bakery products (Culetu *et al*., 2016) [63]. Polyphenolics in food contains antioxidants with numerous health promoting benefits that can treat cardiovascular diseases, diabetes, neurodegenerative diseases and control weight difficulties. They act as natural antioxidants, natural coloring agents, nutritional additives and conservative agents in food (Munin and Edward-Levy., 2011) [76].

4.3 Application of citrus utilization waste in cosmetic industries

Cosmetic industry intend using citrus waste in their products because citrus waste are good source in preventing and recovering broken skin. Citrus waste can improve the structure and functioning of skin due to its antioxidants protection, synthesizing of collagen, photoprotection properties and anti-inflammatory activity (Pearson, 2018) [64]. Citrus waste comprises of compound like carotenoid, flavonoids, minerals, vitamins, polyphenols and omegas that helps in exhibiting diabetic properties, cancerous activity, allergic and microbial properties in order to formulate and improve better skin tone, nails, hair, and prevent xerosis that causes constant skin dryness due to insufficient oil in the skin. Citrus peel in cosmetic industry help in the synthesizing of melanin through an enzymes called tyrosinase related protein TRP-1 and TRP-2 with microphthalmia-associated transcription factor (MITF) that help in regulating those enzymes (Yen *et al*., 2012) [65]. However, melanin are pigment found in the skin that help in preventing UV rays from damaging the skin. It causes dark colour in the eyes, and skin. The whole processing details of citrus fruit are given in Fig. 6.

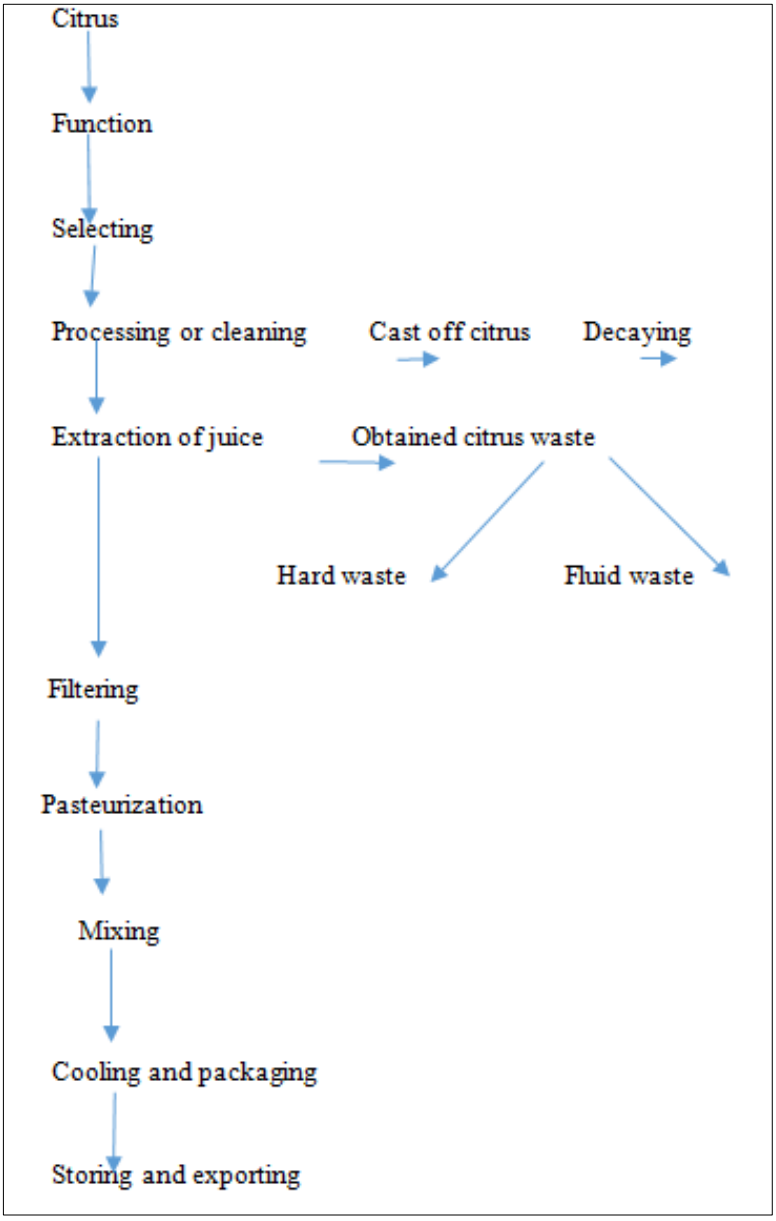

Fig 6: Flowchart showing the processing of citrus

4.3.1 Carotenoids

Carotenoids is a pigment found in citrus responsible for colour change that can be found in food containing red and yellow colour and citrus as well. It has various types like

lutein, beta-carotene, zeaxanthin and lycopene that are mostly used in cosmetic industries due to their abilities in enhancing better skin and scavenging those reactive oxygen species (ROS) (Anunciato and da Rocha Filho, 2012) [66]. Beta carotene is a good source of vitamin A that contribute highly in preventing skin against UV induced erythema and serve as a supplement orally for sun protection and inhibits free radicals (Anunciato and da Rocha Filho, 2012) [66]. Carotenoids are effective in cosmetic products making cosmetic products aesthetic and consumers liking. Antioxidants from carotenoids improve and formulate the maintenance of skin firmness, improving skin tone, and as well guiding skin against the exposure of UV light.

4.3.2 Vitamins

Availability of vitamin also play a major role in cosmetic industry and have an important on the skin. Vitamin acts as hydrophilic potential antioxidant that helps in protecting the skin from absorbing UV light (Taeymans *et al*., 2014) [68]. Niacin which is a vitamin B3 that is available in nuts, fish, milk and egg can promote the production of dermal elasticity and collagen and induce the development of inflammation, stop sunburns, removing wrinkles and acting as a nutrient for antiageing (Draelos *et al*, 2019) [69]. Application of vitamins in cosmetic industry can lowers the formation of androgen and suppresses the activity of sebaceous gland (Pearson, 2018) [64]. Vitamins like niacinamide can stops the yellowish of skin and promote smooth skin texture and as well slows down dyspigmentation of the face through a mechanism that stops the transferring of melanosome from melanocytes to keratinocytes (Hakozaki *et al*., 2002) [67].

4.3.3 Polyphenolics

Polyphenolics acts as an antioxidants in cosmetic industry that helps slower the development of premature aging and oxidative damage. It antioxidants activity helps to gives out photoprotective actions that helps in the preventing or treating sun- stressed skin, oily skin and prevent the deterioration of oxidative constituents of cosmetic (Monteiro e Silva *et al*., 2013) [70]. Polyphenolics are used in cosmetic industry because it constitute antiallergic, antimicrobial and vasoactive properties that serves as ingredients of dermacosmetics for acne sensitive and capillary skin. Cosmetics products like cream containing antioxidants can stops aging and enhances skin tone.

4.4 Animal feed industries

Citrus processing waste or by-product are used in animal feed industries because it constitute a high amount of bioactive compounds and as well acts as a nutritious supplement in animal diet to help prevent the growth of bacteria like: salmonella and Escherichia coli within mixed microorganism ruminal media fluid supplemented with citrus waste (Jennings *et al*., 2013) [108]. Citrus processing waste are important in animal feed industries due to the high amount of structural fiber it contains which helps in providing the require nutrients for production, maintenance, growth and reproduction (Mirzaei and Sis, 2008) [109]. Citrus pulp, citrus molasses, activated citrus sludge, fresh citrus pulp, citrus fines and meal, citrus dried pulp, citrus silage and citrus peel liquor are waste or by-products obtained from citrus that can be used as an important feeds for animal because they are high in energy and promote lactation and support growth in animals with lesser negative effects than feed that is rich in starch (Bampidis and Robinson, 2006) [110].

4.5 Recent trends in citrus processing waste utilization

There have been enormous trends recently that have occurred in the utilization of citrus processing waste and on such a positive basis, industries like pharmaceuticals, food and cosmetic have found interest in utilizing citrus waste in order to add value to their product such as flavouring agents, scavenging free radicals and promoting health. Utilization of citrus waste can be used directly for animal feed, compost, soil conditioner, agronomic utilization, and for extracting high valuable bio-active compounds like: pectin, carotenoids, essential oils, dietary fibre and phenolic. It can also be used for transforming high value added products such as: biogas, anaerobic digestion, fermentation, pectic oligosaccharides, enzymes, bio-ethanol, bio-polymers and thermo chemical process that includes: syngas, gastification, incineration and physico-chemical process like: biodiesel and trans-esterification. The utilization of citrus wastes has contributed in the reduction of environmental problems and also served as a renewable recovery of different bio-based products such as: bio-fuels, enzymes and organic acid (Nizami *et al*., 2017) [29]. Citrus waste has been used as a sustainable environmental material such as: bio-fertilizers, bio-sorbents and nanoparticle. Citrus waste used as a bio-fertilizers serves as a rich sources of carotenoids and phenols that can be used to improve the shelf life of beverage and food (Okino Delgado and Flueri, 2016) [30]. When citrus waste are chemically used as a bio-sorbents, microfibers cellulose or pectin that are extracted can be used for the removal of radioactive elements Sr (II) and Cs (I) via cation mechanism exchange (Pangeni *et al*., 2014) [31]. Citrus waste used as a nanoparticle, it pectin obtained can be used for making microsphere and as a producing substrate for nano bacterial cellulose (Fan *et al*., 2016, and Zhang and Zhou, 2017) [32, 33]. Citrus waste has played an important role in bio-refinery products. It waste has been utilized in producing an enzymes like xylanase and pectinase that amounted a total yield of 265 U/g and 65 U/g from aspergillus niger through the process of solid state fermentation under a specific intensity of air flow of 1 V/kg M (Rodriguez-Fernandez *et al*., 2011) [34]. It contributes enormously in the production of pectinase. Citrus waste can also be exploited in the preparation of pectic oligosaccharides through the process of enzymatic hydrolysis by means of purification and membrane filtration (Gomez *et al* 2016) [35]. It can serve as a promising source for the pectic oligosaccharide production. In biodiesel, citrus waste contribute to it production especially in it trans-esterification that highly involve oil that are or can be produce from the seeds of citrus. Citrus waste present in biodiesel help it to be more biodegradable and nontoxic due to its high level of antioxidants and polyphenols. Citrus waste has also been used in the production of biopolymers, biofuels, biogas and bioethanol.

4.6 Future outlook

Citrus processing waste are which are good source of natural supplements obtained from plants are gradually taking the place of food containing chemical as many people are becoming aware of the potential health benefits it has when it has been consumed. In the near future, there will be an

increase demand for food containing natural ingredients due to its strong plant derived nutraceuticals that will take the place of costly synthetic food materials. The managing of waste gathered from citrus which is a good source of functional compounds and its application in various places like food industries, cosmetic industries and pharmaceuticals industries has been given an increase attention due to its enormous and promising health benefits that it possess. The demand for citrus processed waste will increase in the nearby future because many people will already be cognizant about it benefits and will consider utilizing it into many products apart from just food, cosmetic and pharmaceuticals products. Exploiting of citrus processing waste will yield in value added chemicals for stopping environmental damages and may as well helps in the reduction of too many garbage because people will now consider utilizing it waste rather than just discarding or disposing it.

4.7 Conclusion

To conclusively conclude, citrus residue (wastewater and peel) are very essential in various areas especially in pharmaceuticals, cosmetic and food industries. Based on how monumental citrus waste are there should be an increase attention given to it in order to help manage it waste and maximize profit economically. Waste obtained from citrus processing can improve nutrient content and organic matter of agricultural soil with the use of citrus biomass as a non-synthetic conditioner for the production of compost precisely in agricultural areas. It can also be used as a feed for animals. Citrus processing waste has been known to be a good source of inhibiting various sicknesses such as: (inflammation, fungus, bacterial, thrombotic, carcinogenic, acne etc.) because of the availability of various bioactive compounds such as: dietary fibre, limonoids, pectins, flavonoids, carotenoids and essential oils which are all potential sources of improving health. The disposing of waste gathered from citrus may as well have constraint both on environmental and economic factors because they contain high level of essential oil and high water content. Pulp that is produce from citrus through the adsorption technique serve as an effective agent for removing chemicals and metals in an effluent generated by industries.

Based on the promising health benefits and uses of citrus processing waste, I want to strongly use this medium to urge people to stop discarding citrus waste and help enlighten other people about its promising uses and benefits which will also help in the reduction of garbage, promote better health and minimizes the uses of too much synthetic products.

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