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Review

Challenges and opportunities on vegetable oils derived systems for biomedical applications

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ABSTRACT

Vegetable oils have been suggested in polymer science as an environmentally friendly feedstock existing in abundance in nature, with worldwide availability and low cost. Although they have been widely explored as building blocks for polymers synthesis, their functional roles as owners of potent biomolecules are less unexplored. Their ancient biomolecules support natural biological roles such as antioxidant, antibacterial, anti-inflammatory, and anti-tumor properties, which are considered a great promise for biomedical proposes. This comprehensive review provides an overview of grape, soybean, castor, sesame, olive vegetable oils where their native anti-inflammatory, anti-tumor, antioxidant, and antibacterial biological compounds bring health benefits that can be translated to the biomedical field. These plant oils are considered the most relevant for the molecular design of functional and high-performance biomaterials that can contribute to the reduction of carbon footprint. The representative examples of vegetable oil-derived biomaterials, their main composition, shape, and the processing technology will be covered and innovative strategies toward the development of new multifunctional polymeric materials for pharmacological patches, wound healing devices, drug carriers, and scaffolds for tissue engineering applications will be discussed.

Contents

1. Introduction

Currently, the main challenge in polymer science is to maximize the use of renewable bio-resources reducing the environmental and social impact [1–4]. There is a growing body of literature that recognizes the importance

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of vegetable oils (VOs) as renewal environmentally friendly feedstock existing in abundance in nature (e.g., production between 2018 and 2019 was about 188 million tons [5]), with worldwide availability and low cost [2,3,6]. VOS are isolated from seeds, nuts, cereal grains, and fruits [4,7] but can also be obtained as a commodity in the food industry. As seeds are often referred to as significant agricultural and industrial waste, finding feasible solutions for treating this residue, including attempts to develop new materials, would constitute an excellent opportunity [8]. Vegetable oils are usually classified as fixed and essential oils [9], with fixed oils being characterized by being non-volatile, while essential oils are volatile at room temperature. The main constitution of fixed VOs is different proportions of triglyceride molecules, esters of glycerol, and fatty acids (monounsaturated, polyunsaturated, and saturated) [4,8,13,14]. As shown in Fig. 1(A), triglycerides are formed from the esterification of glycerol, and three fatty acids contribute to 95% of their total weight [13,14]. VOs exhibit distinct composition, bonds stereochemistry, chain lengths, and degree of unsaturation that is characteristic and considered a fingerprint of each oil. The presence of specific reactive functional groups in VOs fatty acid structure allows the direct use of VOs in polymer synthesis [1,4,15], where chemical modification of triglycerides reactive sites has been widely used to develop novel routes of polymer production [1,4,15,23]. The chemical structures and fatty acid composition of the most studied VOs are presented in Fig. 1(B), where soy, palm, castor, linseed, and sunflower [16] oil are the oils most used for polymers production [17,18]. Resuming the available scientific literature reveals that multi-functional polymer synthesis from VOs is technologically possible where 2D and 3D structures [24,25] were achieved and are applied in adhesives, paints, and coatings [1,15,26]. Besides the advantage of being used in polymer synthesis, VOs present multiple and unique bioactive biomolecules that are considered major building blocks of life, opening their possible applications in the development of novel biomaterials for biomedical applications [20,21].

The novel chemical and biological properties of VOs biomolecules can play an important role in the construction of novel biomaterials either by direct processing or combining them with natural and/or synthetic

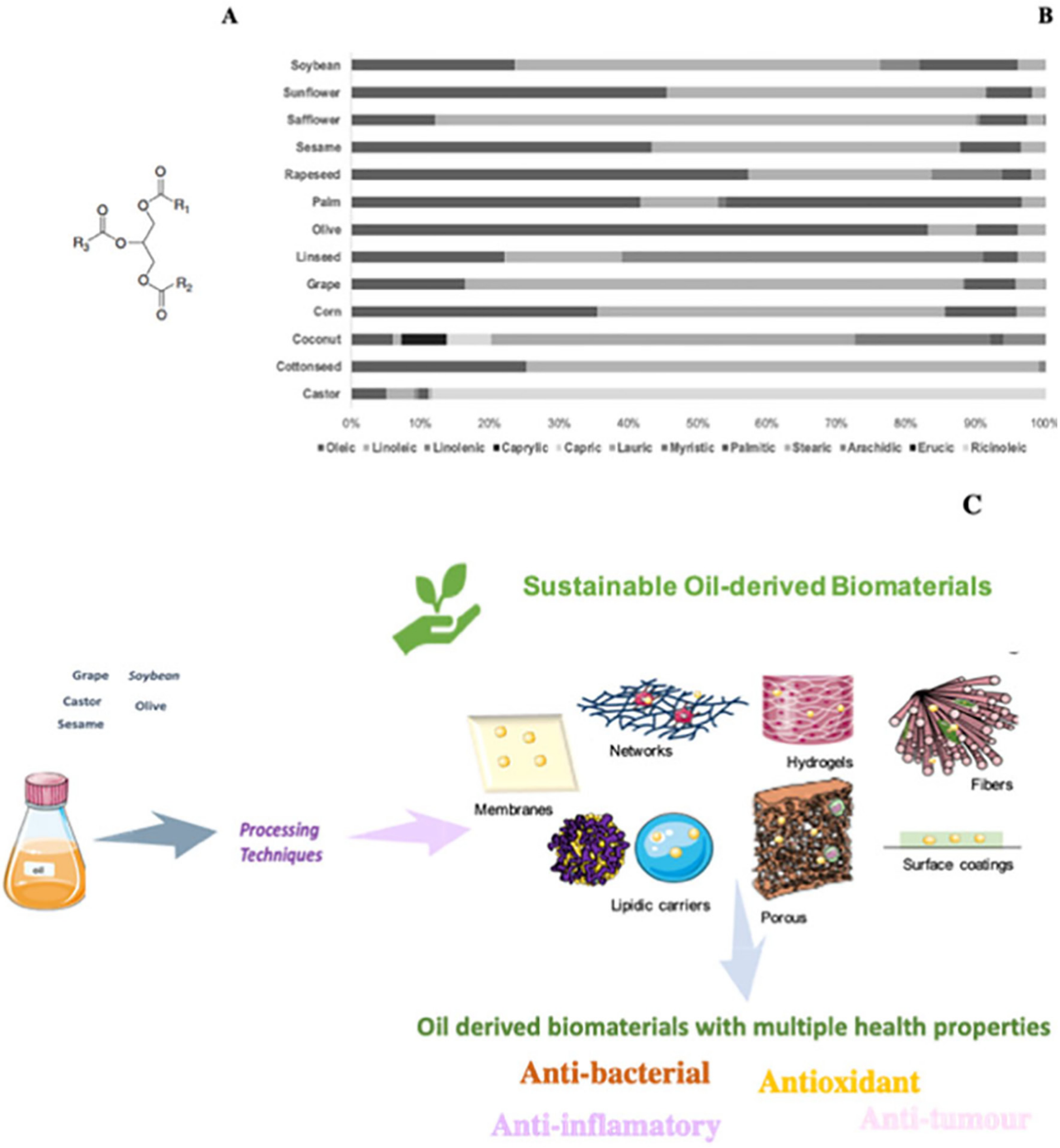

Fig. 1. (A) General vegetable oil triglyceride structure [27], (B) fatty acid percentage and composition of most studied vegetable oils, and (C) scheme regarding the development of sustainable oil-derived biomaterials.

materials (Fig. 1(C)). This concept of using existing naturally derived biomolecules of plants and animals is considered an emergent area in tissue engineering (TE) that provides a low-cost and sustainable approach that benefits the economy and environment while providing unique biological advantages. The specific properties that make VOs attractive for biomedical applications are their inherent biological nature that favors biomolecular recognition, responsiveness to biological stimuli, biocompatibility, and biodegradation. They degrade under physiological conditions and are well metabolized by the human body without toxic consequences. Besides that, VOs harbors multiple unique biomolecules with potent anti-inflammatory, antioxidant, antibacterial, and anticancer features, among others [9,10,27–31]. Many of these molecules are overlooked and understudied for biomedical proposes, partially due to their simplicity. However, as we continue studying their physical, chemical, and biological properties, we discover additional functionalities that can exploit the development of cost-effective natural-based biomaterials, with a reduced carbon footprint and superior biocompatibility for applications that include pharmacological patches, wound healing devices, drug carriers, and scaffolds for TE as well as regenerative medicine [2,12,32,33]. One relevant concern is attributed to the contamination of VOs with potentially toxic elements resulting from impurities (metals and pesticides) that naturally occur in the environment. However, recently it was concluded that the concentration of potentially toxic elements in VOs does not pose a risk for the health of consumers, confirming that from the safety point of view, vegetable oils are nontoxic and safe to be used in biomedical processes. The fact that most of VOs are considered safe food additives by the Food and Drug Administration encourages a possible faster clinical translation of VOs based biomaterials. The existing review articles dealing with VOs, focus on vegetable-based polymers chemistry and synthesis [1,4,15,23], however, the major goal of this article is to present a significant report from literature to provide an enchanting perception of vegetable oil-derived biomaterials. In this article, five distinct oils (grape, soybean, castor, sesame, olive) were selected since it was already proved that they provide health benefits (nutritional and cosmeceutical) against many diseases and because there is preliminary evidence of their function in biomedical applications [1,2,4,10,16]. An in-depth and critical discussion on the design, fabrication, and applications of VOs-derived biomaterials is presented by considering appropriate and important examples of each oil type. We intend to finish proposing novel strategies and future perspectives toward the development of novel oil-derived polymeric biomaterials systems for biomedical purposes.

2. Vegetable oils multiple biomolecules and biological properties

Grapeseed oil is a wine by-product extracted from seeds of grapes using mechanical methods or organic solvents [1,10,34]. It is constituted by fatty acids (linoleic acid most abundant, oleic), phenolic compounds (flavonoids, carotenoids, phenolic acids, tannins, and stilbenes), vitamin E (tocopherol and tocotrienol), polyphenols (catechins, epicatechins, trans-resveratrol, and procyanidin B1) and phytosterols among others [58]. Grapeseed oil tocopherols are considered one of the most powerful oil-soluble antioxidants. The health benefits of linoleic and linolenic acid abundant fatty acids include cholesterol and hypertension reduction, providing cardio-protection as well as preventing cancer and autoimmune diseases [8,22,35–37]. The antioxidant, anti-inflammatory, and photoprotective properties of grape oil polyphenols are known to protect against UVB-induced skin inflammation, oxidative stress, and skin cancer (e.g., melanoma) [35,38]. Besides that, topical application of grapeseed oil protect the skin barrier function [9], inducing a faster wound healing with a greater connective tissue deposition [9,22,39]. Table 1 displays VOs bioactive molecules with their main health benefits resulting from in vitro, in vivo, and human clinical trials of VOs ingestion and topical application.

Soybean oil is extracted from seeds of *Glycine max*, and it is considered one of the in-expensive major sources of edible oil in the world. It is constituted of linoleic acid, oleic acid, palmitic acid, alpha-linolenic acid, and stearic acid residues, where 85% of the oil is made of unsaturated fatty acid. The minor components of soybean oil are phospholipids (lecithin), phytosterols, and tocopherols, considered natural antioxidants that maintain cell membranes' integrity and protect them from harmful ROS [3]. Literature with patient's data reveals that phytosterols (B-sitosterol) reduce blood LDL-cholesterol levels by 10 to 15%, decreasing the chances of cardiovascular as well as menopause symptoms. Vitamin K of soyabean oil is an essential element promoting bone formation and neuronal protection in the brain [41]. Soybean oil has been integrated into several skin formulations since its topical application demonstrated a supportive effect in the native lipids of the stratum corneum, providing a better barrier function with the consequent decrease in human skin transepidermal water loss [42]. The topical application of soybean oil protects against UVB-induced skin inflammation due to tocopherols and polyunsaturated fatty acids that work as radical scavenging [43].

Castor oil, also identified as Oleum Palmae Christi, is isolated from the seeds of *Ricinus communis* that accumulate about 45–55% oil in the form of triacylglycerol. The uniqueness of castor oil is related to its single fatty acid-type in high concentrations consisting of 90% ricinoleic. The high ricinoleic acid content provides chemical versatility, oxidative stability, and high shelf life to the oil [44]. Polyphenols, phytosterols, and tocopherols are one of the natural antioxidants present in castor oil that exert anti-proliferative and anti-inflammatory properties. Some therapeutic properties of castor oil comprise gastrointestinally (naturally derived lubricant important in intestinal dryness) [3,45], antimicrobial [46,47], anti-inflammatory [48,49], analgesic, and lymphatic stimulant [50]. The effect of castor oil in uterus motility is widely described, contributing to labor induction, however with consequent unwanted side effects such as nausea [45,51]. Topical application of castor oil demonstrates a reduction in skin keratosis, dermatosis, acne, and skin infections and promotes wound healing [48].

Sesame (*Sesamum indicum*, L.) belongs to the order Tubiflorae, the family Pedaliaceae. Sesame seeds are consumed worldwide, and their constitution is based on 46%–50% of oil with 83%–90% unsaturated fatty acids, 20% proteins, vitamins, minerals (calcium, phosphorus, potassium, magnesium, sodium, and iron), carbohydrates, lignans phytosterols, phytates and other micronutrients [52–55].

The ingestion of sesame oil has demonstrated beneficial effects regarding oxidative stress in patients with osteoarthritis [26]. In ancient times, sesame oil was used to massage the body in different kinds of body pains, namely neuralgia, paralysis, gout and rheumatism, limb trauma [53,54,60], while nowadays it has been mostly used in the pharmaceutical and cosmetic industry (perfumery, soap) [22,53,61]. Clinical tests using massage with sesame oil are an effective complementary method in reducing the pain severity of patients with trauma [60] and chemotherapy-induced phlebitis [62]. A clinical trial with thirty patients with traumatic wounds reveals that the topical application of soybean oil protects against UVB-induced skin inflammation, reduced pain, minimized wound area, and induced skin epithelialization [63]. Although the mechanism is not fully understood, the considerable quantity of lignans, linoleic and palmitic acid can reduce/inhibit prostaglandins and leukotrienes, lightening inflammation and pain [22,60,62]. Sesame oil is also considered a natural sunblock. The known photoprotection results from the presence of sesamol that inhibits UVB-induced ROS generation reduces lipid peroxidation, and thiobarbituric acid reactive substances, thus preventing photodamage [64] postponing the skin aging process by slowing down the oxidation in skin cells [65]. Olive oil comes from *Olea europaea* tree, and it is constituted by 98% of fatty acids (palmitic acid, oleic acid, linoleic acid, linolenic acid, with oleic acid being the predominant), and the residual 2% are an unsaponifiable fraction (squalene, carotenoids, sterols, terpenic, aliphatic alcohols, phenolic, and other minor compounds) [23,56–59]. The nutraceutical and pharmaceutical benefits of olive oil belong to its fatty acids and the principal minor phenolic component. Olive oil modulates the inflammatory process associated with the immune system, with extra virgin olive oil with its phenol content presenting important antioxidant properties. Olive oil ingestion is known to prevent hypertension, obesity, hypercholesterolemia, and consequent cardiovascular diseases, diabetes mellitus type 2, cancer [66,67], inflammation-mediated disorders (such as osteoarthritis),

Table 1
Vegetable oil's main composition, bioactive molecules, and biological properties.

Vegetable oil	Composition	Main bioactive molecules	Biological properties
Grape	Fatty acids Phenolic compounds Vitamin E Polyphenols Phytosterols [58]	Resveratrol Tannins Gallic acid Proanthocyanidins Procyanidins Vitamin E [58]	Antioxidant: GA, EC, CAT, PAs, PCs and Vit. E inhibit lipid peroxidation, scavenging free radicals and metals chelation [36] Anti-inflammatory: *PPs* inhibit arachidonic acid cascade which activates inflammatory response [38,39] Antimicrobial: RES induce oxidative damage to bacterial membrane (e.g. *S. aureus* and *E. coli*) not compromising host cells [37,40–42] Antitumor: PAs act on breast [38,43], colon [44,45] and prostate [46] cancer [44,45,47,48]. Cell cycle regulation [48,49], VEGF and angiopoietins attenuation [44], PI3-kinase pathway suppression inducing cancer cells apoptosis [44,45]. TTs induce apoptosis of breast and colon cancer cells [36,50] Chemoprevention: PAs extract upregulateBcl-2 and down regulation of c-myc and p53 genes of chang liver epithelial cells [48] Photoprotection: PAs absorb and dissipate UV radiation and acts against UV radiation induced inflammation and oxidative stress [51]
Soybean	Fatty acids Isoflavones Vitamin E Vitamin K Phytosterols [3,52]	Linoleic acid Genistein Daidzein Phytosterols Tocopherols [3,52]	Antioxidant: PS, TC and TTs [3,52] present radical scavenging activity, antioxidant enzymes expression; quenching lipid peroxyl radicals [53] Photoprotective and anti-inflammatory: TC and PUFA work as radical scavenging protecting against UVB induced skin inflammation [54] Osteoblastogenesis: GEN and DAI increase ALP and type I collagen via MEK/ERK and PI3 K/Akt pathways resulting in osteoblastogenesis [55] Other: heart diseases prevention, vitamin K provides neuronal protection, although the mechanisms are not yet understood [30].
Castor	Fatty acids Allergenic proteins Ricin [56–58]	Ricinoleic acid	Anti-inflammatory: RA with potential interaction with sensory neuropeptide-mediated neurogenic inflammation (mechanism under study) [58] Antimicrobial: R and S configured RA amides promote membrane bacteria damage (*S. aureus*, *A. brasiliensis* and *Penicillium*, *B. subtilis*) [57] Antinociceptive: local depletion of substance P by RA [58] Laxative and labor inducer: RA is a natural intestinal lubricant and stimulator of uterus motility through activation of EP3 receptors on smooth muscle cells [56]
Sesame	Fatty acids [59,60] Vitamin E Lignans Phytosterols [61]	Sesamol Sesamin Sesamolin Sesamino	Antioxidant: Ses, SES, Sesa, SML and TC modulate antioxidant enzymes, oxidative stress markers, and lipid peroxidation reducing superoxide production [62] Anti-inflammatory: Ses, SES, Sesa and sesamino [62] decrease pro-inflammatory cytokines and/or ROS production, induction of antioxidative enzymes activity, downregulation of caspase 3; inhibition of arachidonic acid cascade [63] Antitumor: Ses and SES demonstrate anti: proliferative, inflammatory, metastatic, angiogenic properties as well as pro: apoptotic and auto phagocytic activities [64] Chemoprevention: Ses protects against pancreatic, lung, breast, liver, colon and skin cancer [65,66], where MAPK and NF-kB, caspase and Nrf2 signaling pathways are activated [65] Antiseptic and anti-hypertensive: SES regulates lipid metabolism, xenobiotics and alcohol at the mRNA level Photoprotective and anti-aging: Ses inhibits UVB induced ROS production; reduces lipid peroxidation and thiobarbituric acid reactive substances [51] slowing oxidation [67], preventing skin photo-damage [68]. Anti-wrinkle and anti-aging properties due to high anti-tyrosinase activity [61,69] Anti-nociceptive: activation of micro-opioid receptors [60]
Olive	Fatty acids Phenolic compounds [70] Polar pigments Triterpenic dialcohols Sterols Tocopherols Hydrocarbons Xanthophylls [25,71–74]	Carotenoids Squalene Tocopherols Phenolic compounds	Antioxidant: Ty, HT, FL, OE, OC, Car, SQ and TC with radical scavenging activities preventing lipid oxidation [75] Anti-inflammatory: PC modulate pro-inflammatory, gene expression and cytokines secretion [15,76,77], attenuation of TNFα, interleukin 1β and inducible nitric oxide synthase [10,74] Antimicrobial: OA, OC, HT and TY decrease intracellular ATP, promote cell depolarization, damage and reduction of bacterial DNA [10,78]. OC prevent the growth of *H. pylori* associated with peptic ulcer and gastric cancer development [72,74,79] Antitumor: OA, PPs and flavonoids hindered cancer cells proliferation [72,74]. HT and Ty reduce the skin cancer incidence [24]. High doses HT induce cell cycle arrest and apoptosis colon and thyroid cancer cells Chemopreventive: inhibition of endothelial cell proliferation, migration and invasion, modulation of arachidonic metabolism and reduction of NF-kB, Wnt/β-catenin, P3IK/akt, SAT3 [80] Chondroprotective effect: PPs induce autophagy and suppression of inflammation [81]

Abbreviations: RES - resveratrol; GA - gallic acid; EC – epicatechin, CAT – catechin; PAs - proanthocyanidins; PCs - procyanidins; Vit. E - vitamin E; PPs - polyphenols; *S. aureus - Staphylococcus aureus*; *E. coli - Escherichia coli*; VEG - vascular endothelial growth; TTs - tocotrienols; PS - phytosterols; TC - tocopherols; PUFA - polyunsaturated fatty acids; GEN - genistein; DAI - daidzein; ALP - alkaline phosphatase activity; RA - ricinoleic acid; *A. brasiliensis - Aspergillus brasiliensis*; *Penicillium - Penicillium expansum*; *B. subtilis – Bacillus subtilis*; Ses - sesamol; SES - sesamin, Sesa - sesamolin, SML - sesaminol; Ty - tyrosol; HT - hydroxytyrosol; FL - flavonoids; OE - oleuropein; OC - oleocanthal; Car - carotenoids; SQ - squalene; PC - phenolic compounds; OA - oleuropein aglycone, OC - oleocanthal; *H. pylori - Helicobacter pylori*.

and metabolic syndrome [56–58,68,69]. Epidemiological studies have also shown that olive oil consumption is associated with a reduction of breast cancer risk [66,67]. Biophenolic extracts tested in NIH-3T3 cell line contribute to the recovery of cell oxidative stress [58] where oleuropein, phenols, and flavonoids, besides the strong antioxidant potency, hindered cancer cells proliferation [57,59]. Oleocanthal demonstrated anti-proliferative actions, inducing cell apoptosis by activating caspase-3 and poly-adenosine diphosphate-ribose polymerase, phosphorylation of p53, and destruction of DNA in human colon adenocarcinoma cells [57]. Hydroxytyrosol and tyrosol from olive oil have also demonstrated the ability to prevent human keratinocytes death upon exposure to UVB, reducing the incidence of skin cancer [22] and suggesting that these biomolecules play a potential role in preventing skin damage [70]. Topical application of the oil improves hydration, exerting a protective [122] effect, and stimulating physio-logical protecting and repairing mechanisms of skin [71]. The high level of squalane (from olive oil) in some products protects the sensitive lipids of skin, working as a natural sun blocker. Resuming, the chemical composition and the oligomeric character of VOs can strongly favor the development of novel biobased biomaterials with different physicochemical characteristics.

3. Development of vegetable oil-derived biomaterials

In the past decades, progressions in the biomedical field have made it possible to design and construct biomolecules-derived biomaterials. The processing and modification of biomolecules and/or their integration with other natural and/or synthetic materials lead to the development of varied chemical, physical, mechanical, and biomimetic properties to generate responsive biomaterials and devices. As it was possible to understand, the reviewed VOs have in their constitution a diversity of unique biomolecules that can offer a source of inspiration for bio-materials design. Although some efforts have been made to develop VOs system (films, particles, fibrous, and gels structures) described in the next section, we consider a research field in its infancy with unlimited prospects. Natural origin materials such as chitosan and alginate are the biopolymers mostly combined with VOs [50,72,73], due to their proven excellent biocompatibility; however, synthetic polymers such as polyurethane were also employed [74–77] due to their well-known mechanical resistance, excellent biodegradability, and biocompatibility. Enhanced bioactivity, biocompatibility, biodegradability, stability, and sustainability are perceived advantages of oil-derived biomaterials, where the main applications are mostly in wound healing patches, drug delivery systems, and scaffolds for TE (see Table 2). Many oil-based biomaterials are being translated from the food industry, where their bioactivity, rheological, and facile gelation have garnered significant interest. However, care should be taken with the harsh chemical processing conditions that can further compromise biocompatibility. The degree of heterogeneity in biomaterial physicochemical properties observed in this review also reflects the need to optimize the main properties to match the demands of the target tissue type. As such, an anticipated characterization is warranted before considering their application for clinical use.

3.1. Vegetable oil-based films/membranes

Thin polymeric films are widely used in wound dressings since they trap exudates, prevent bacterial infection, and deliver a moist environment for wound healing. Taking that into consideration, Díez-Pascua et al. explored the antibacterial properties of castor oil, zinc oxide nanoparticles (ZnO NPs), and chitosan to produce antibacterial films. ZnO NPs and castor oil were dispersed in a chitosan matrix, and films were extensively characterized. The novel non-toxic and environmentally friendly films (see Fig. 2) showed improved mechanical properties, biocompatibility, biodegradability, and antibacterial efficiency in the presence and the absence of UV light. In vivo healing studies demonstrated that films induced faster-wound healing, promoting re-epithelialization and collagen deposition due to castor oil healing properties, thus displaying potential for wound dressings [50]. Tavolaro et al. monitor the beneficial antitumor effects of extra virgin oil on human breast cancer cells seeded in zeolite membranes produced using polylactide acid with pure and hybrid synthetic zeolite particles [67]. Results demonstrated that the virgin olive oil stimulated apoptosis in both human breast cancer cell lines (MCF-7 and MDA-MB-231), due to oil phenols [58,67,68]. It is important to refer that one of the main drawbacks of working with VOs incorporation in films is oil droplets agglomeration. It is recommended to obtain a homogeneous distribution of VOs droplets in films via a probe-type ultrasonic homogenizer. It is also important to achieve the percentage of VOs in the polymer matrix since high VCOs percentage has been shown to reduce protein adsorption and consequently inhibit cell adhesion [78–80].

3.2. Vegetable oil-based particle systems

At the moment, encapsulation of drugs in natural and synthetic polymers is considered as an interesting approach to i) preserve molecules from oxidation reactions with the environment, ii) modulate drug release efficacy, iii) improve physical stability, iv) enhance bioactivity, and v) reduce toxicity [81]. Although there are several encapsulation strategies in pharmaceutical sciences, the available templates based on VOs include

Table 2
Preparation of vegetable oils derived biomaterials, main outcomes, and potential biomedical applications.

Oil type	Composition/shape	Processing/technology	Main outcomes	Biomedical applications
Grape	PUR fibrous scaffold, grape oil, honey and propolis	Electrospinning	Non-toxic effect against red blood cells and human fibroblast cells; delayed blood clotting time	Bone TE [88]
	Alginate-gelatin hybrid nanoparticles	Emulsification	Induction of keratinocytes proliferation and ECM synthesis with drug release profile over 2-weeks	Drug delivery, TE and RM [95]
	Grape, fish and laurel leaf oil lipidic careers	Emulsification Lyophilization	Antioxidant activity inducing a decrease in cervical, breast and melanoma cells proliferation	Antitumor drugs [33]
Soybean	Soybean oil-g-polystyrene membranes	Solvent casting	Enhanced proliferation and differentiation of pre-osteoblastic cells	Bone TE [30]
	Soybean oil and sebacic acid films/porous scaffolds	Solvent casting/salt leaching	Cytocompatible, inducing stem cells proliferation and osteogenic differentiation.	Bone TE [28]
	Soybean oil epoxidized acrylate scaffolds	Stereolithography/printing	Shape memory effect, cytocompatible, supporting growth of human bone marrow MSC	TE [100]
	Epoxy resins from trehalose, cyclodextrin, soybean oil	Solvent casting	Cyclodextrin films-tunable mechanical properties, nHDF adhesion/proliferation. Trehalose based films inhibit cell adhesion/growth	Adhesives, antifouling coatings to wound healing and TE [101]
	Soybean oil-based polyurethane networks	Solvent casting	Mouse fibroblast cells showed good adhesion and growth behavior	Biomedical [102]
	α-Cellulose and epoxidized soybean oil	Solvent exchange/freeze-drying	Scaffolds support fibroblasts and pre-osteoblasts cells attachment and proliferation	TE [103]
Castor	Electrospun polyurethane, castor oil nanocomposite	Electrospinning	Scaffolds with anticoagulant properties and low hemolytic index	Vascular graft applications [97]
	Castor oil/silica hybrid particles	Emulsification	Cytocompatibility and biodegradable by lipase with liberation of ibuprofen	Drug delivery vehicle [104]
	Polyethylated castor oil-based paclitaxel NPs	Not described	Efficient transport drugs to tumors	Drug delivery for breast cancer [163]
	Castor oil-based elastomer	Solvent casting	In vitro and in vivo studies proved that degradation products were biodegradable and biocompatible	TE and drug delivery systems [23]
Sesame	Sesame oil microemulsion based hydrogel	Microemulsion	Reduce skin damage upon sunlight exposure	Skin cosmetics [68]
	Polyurethane, sesame oil, propolis, honey scaffold	Electrospinning	Reduced toxicity against red blood cells and enhanced cell viability for HDF	Skin TE [99]
	Sorbitan monostearate–sesame oil organogels	Dissolution	Biocompatible with metronidazole-loaded organogels showing antimicrobial activity (*E. coli*)	Topical drug delivery for skin [107]
	Bigels obtained by guar gum hydrogel and sorbitan monostearate sesame oil	Dissolution	Biocompatible, drug release prolife and antimicrobial efficiency (*B. subtilis*)	Topical drug delivery [108]
	Bigels using sorbitan monostearate-sesame oil organogel and carbopol 934 hydrogel	Dissolution	Biocompatible, efficient drug release, antimicrobial efficacy (*E. coli*)	Vaginal drug delivery vehicles [109]
Olive	Olive oil/PUR blends with silver NPs	Electrospinning	Bionanocomposite inhibit *E. coli* growth and display non-cytotoxic behavior against fibroblasts	Bandages for skin diseases [98]
	PUR nanofibrous composite, olive oil, honey, and propolis	Electrospinning	Reduced hemolytic index and non-toxic behavior against human dermal fibroblasts	Bone TE [96].
	Olive oil lipid carriers, eucalyptus oil	High shear homogenization	Cytocompatible, induced fibroblasts proliferation and exhibit antimicrobial properties	Wound healing, dermal infections [110]

Abbreviations: PUR – polyurethane; ECM - extracellular matrix; MSC - mesenchymal stem cell; nHDF - neonatal human dermal f fibroblast; NPs - nanoparticle.

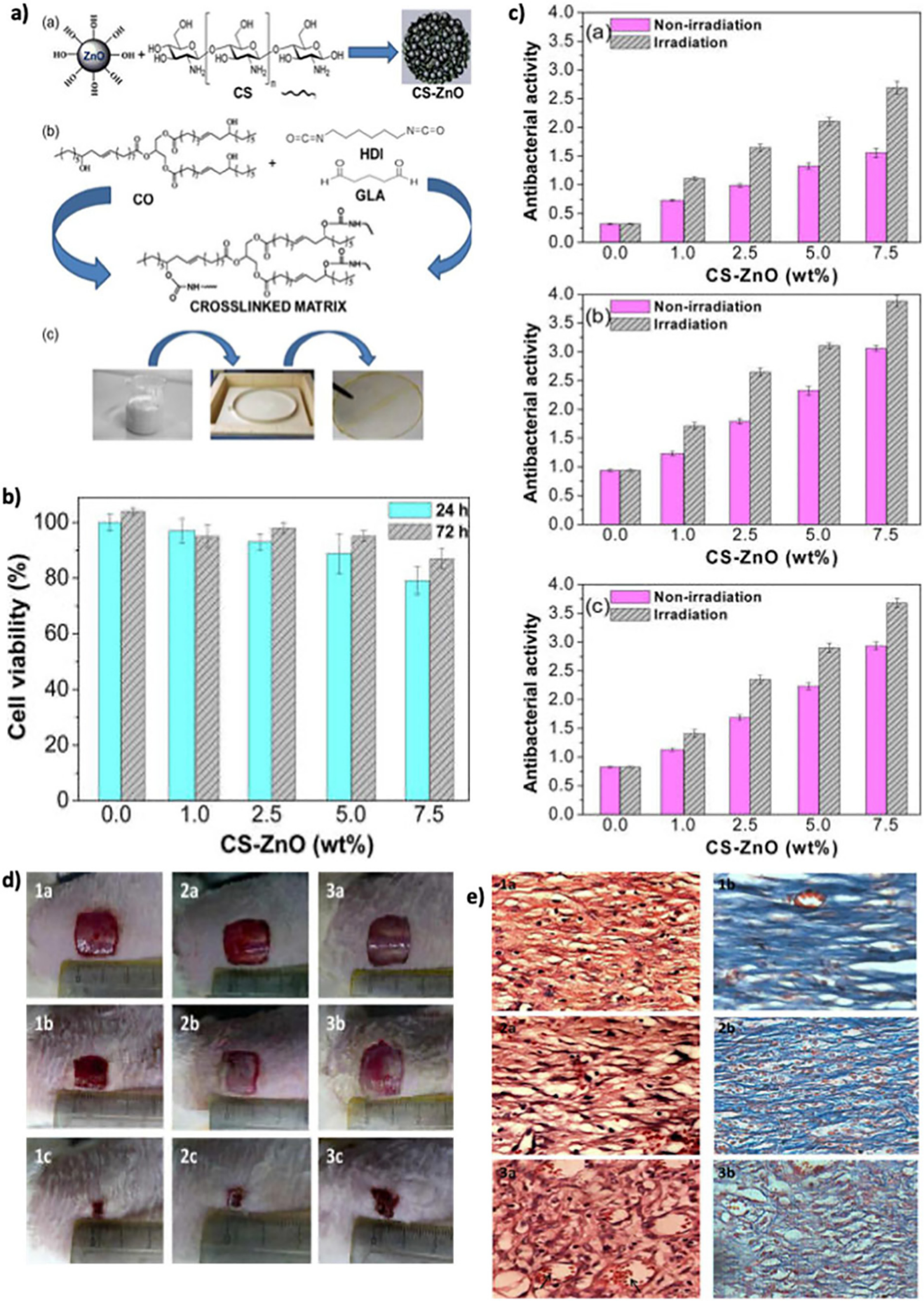

Fig. 2. Schematic representation of (a) chitosan, ZnO nanoparticles, the crosslinked matrix, and film casting procedure. (b) Human dermal fibroblasts viability and (c) antibacterial activity of films against *E. coli*, *S. aureus*, and *M. luteus* without and with UV light irradiation; (d) photographs of the wounds treated with films ((1) CO/CS-ZnO (5.0 wt%), (2) CO, and (3) gauze as control at day 0 (a), day 5 (b), and day 14 (c) and their (e) correspondent histological sections).
Reprinted with permission from f [50].

hybrid particles, nanoparticles, and emulsions mostly applied as drug delivery systems for cancer and topical structures for wound healing applications (see Fig. 3). Castor oil/silica hybrid microparticles seem to be an efficient system to deliver and encapsulate poorly water-soluble drugs such as ibuprofen (Fig. 3(A)). The system showed a good in vitro degradability (digestion using lipases) with a tunable release during 3 h in simulated oral administration dependent on the oil-silica ratio. The microparticles were demonstrated to be cytocompatible against fibroblasts and enterocyte-like cells, showing their ability as delivery systems for health-related diseases treated with ibuprofen [82]. A targeted drug delivery system, which releases the drug at a preselected site in a controlled manner, is a conventional strategy in anticancer targeting and treatment. To enhance drug delivery and improve safety in the drug delivery process along with patient compliance, bio-compatible alginate gelatin nanoparticles were synthesized using grape oil by water emulsification technique [72,81]. The electrostatic bonds between alginate and gelatin give rise to a controlled release of doxorubicin, a synthetic drug with anticancer activity. Interestingly, the viability of human keratinocytes was not compromised, demonstrating that grape oil does not compromise the biocompatibility of the hybrid system, since gelatin and alginate biocompatibility is widely proved [72]. However, not all VOs are considered fully biocompatible; for example, polyethylated castor oil stimulated toxicities in cancer patients. To overcome the toxicity implied by polyethylated castor oil, new nanoparticles of albumin-bound paclitaxel were synthesized for breast cancer women treatment since paclitaxel plays an essential role in breast cancer [83,84]. The clinical trial results demonstrated that solvent-castor oil-based paclitaxel limitations were overcome by albumin-bound paclitaxel nanoparticles that show a higher efficiency preferentially to transport drugs to tumors without the need of premedication [83,84]. It is important to refer that the biocompatibility of castor oil, as any other oil always depends on the dose and that ricin, one of the most toxic substances of castor oil, is eliminated during oil extraction. One of the main drawbacks of synthetic drugs is their possible systemic toxicity and side effects with chances that cancer might recur. These paradigm shift research, and nowadays, the introduction of oil anti-tumor molecules to develop drug delivery systems for cancer is considered a Modern Era of Ancient Medicine. The new formulations have demonstrated remarkable improvement in stability, solubility, sustained release profile, targeted delivery, improved therapeutic efficacy, and reduced toxicity. One example is the use of the intrinsic anti-tumor properties of grape seed and laurel leaf oil that were applied to develop lipid nanocarriers. The unique composition of both oils induced multiple cellular responses (e.g., antioxidant activity, induction of cell cycle arrest and apoptosis, modulation of antioxidant enzymes), decreasing human breast and cervical tumor cell proliferation without the need for a synthetic drug [85].

Although the initial positive results of VOs biomolecules triggering multiple anticancer responses, efforts should continue to analyze different VOs and evaluate in vivo, ex-vivo, and in humans to translate into a successful

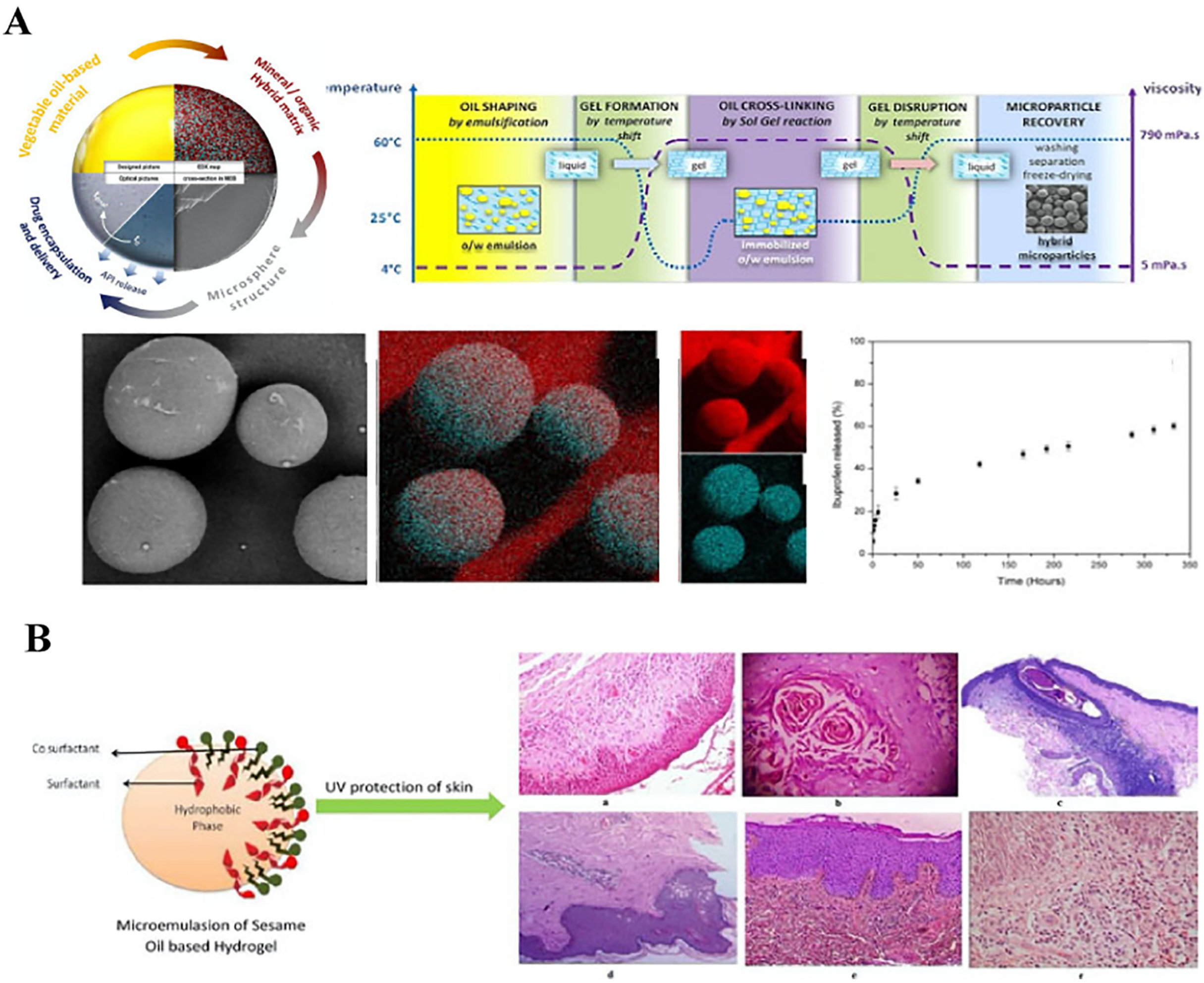

Fig. 3. Oil-based engineering encapsulation systems: (A) castor oil/silica hybrid microparticles produced by thermo-stabilized oil-in-water emulsion process with SEM image of the particle surface with EDX analysis of carbon/silicium map and release kinetics of 4 wt% ibuprofen-loaded microparticles in PBS [82]. (B) Sesame oil microemulsion based hydrogel for UV protection of skin with histopathological analysis of guinea pig's dermal vascular hyperemia, keratin pearls, folliculitis, and perifolliculitis, epidermal hypopigmentation and hyperplasia, focal hyperkeratosis and epidermal hyperplasia and edema and infiltration of inflammatory cells.
Reprinted with permission [64].

outcome. The application of oil-in-water emulsions in cosmetics applications (body lotions and sunscreens) is widely reported [86]. These systems are thermodynamically and kinetically stable, can be administered by various routes (oral, topical, and transdermal), and can deliver hydrophilic as well as lipophilic drugs. The physical properties of the oil phase have an impact on nanoemulsion formation and stabilization and should be very well optimized. For example, nanostructured sesame and olive oil in water emulsions for topical delivery of protein drugs extracted from medicinal leech tissue have been developed [86]. After testing different oil %, a nanoemulsion with 25% olive oil was selected due to its smaller droplet size and physical stability that promotes a better dispersion of the protein drug, therefore, allowing their use as a drug delivery system [86]. The photoprotective properties of sesame oil have also been in skin applications. A micro emulsion-based hydrogel containing sesame oil was explored to prevent the harmful effects of ultraviolet radiation on the skin (Fig. 3(B)). The microemulsion formulation with high sesame oil content, reduced particle size, and high stability was used to synthesize the hydrogel. Histopathological analysis of guinea pig's skin reveals that topical application of micro emulsion-based hydrogel of sesame oil avoids skin damage stimulated by UV radiation. These results are a consequence of the well-known antioxidant and anti-inflammatory properties of sesame oil and sesamin [64]. Nanostructured lipid carrier systems for topical application of sesamol was also developed by Puglia et al. [73] where a combination of two different oil phase (Miglyol® 812 and sesame oil) was used. Results demonstrate that sesamol was successfully encapsulated, with the in vitro data showing a controlled rate of sesamol diffusion through the skin where a prolonged antioxidant activity was achieved [73]. Besides the mixture of different fixed VOs, the mixture of multiple non-essential and essential oils is also technologically possible. Nanostructured lipid carriers based on natural lipids (cocoa butter, as solid lipid, and olive oil or sesame oil) loaded with eucalyptus or rosemary essential oils were developed and applied in skin wound healing. All the nanostructured lipid carriers showed improved biocompatibility and wound healing capacity. The combination of olive oil (high oleic acid content) with eucalyptus oil reveals their synergic effect regarding antimicrobial activity (*Staphylococcus aureus* and *Streptococcus pyogenes*) and wound repair promotion [87].

3.3. Vegetable oil-based fibrous scaffolds

Polymeric nanofibers have a wide range of biomedical applications since they can produce scaffolds with structural similarity, mechanical stability, highly interconnected pores (improving cell-scaffold interaction) resembling native extracellular matrix. A base of honey (anti-microbial and antioxidant activities) and propolis (antibacterial, antifungal, antioxidant, and anti-inflammatory) in polyurethane fibrous scaffolds were combined with success with grape seed oil [88], olive [74], and sesame oil [77] independently for bone and skin tissue engineering proposes. The hemolytic assays and cytocompatibility studies revealed that the electrospun scaffold presents superior blood compatibility and human dermal fibroblasts viability rates. Olive oil anti-microbial activity and effect on physiological skin-repairing mechanisms [71] were also used to develop polyethylene oxide/chitosan/poly(ε-caprolactone)/olive oil composite nanofibers for treatment of dermal infections and burns. The system was demonstrated to be biocompatible and exert antimicrobial activity [89]. Although the doping of fibrous systems with VOs induced anti-bacterial properties, the efficacy is sometimes limited. Considering that organic and inorganic particles that have been widely used in the biomedical field to improve antimicrobial activity can also be employed.

3.4. Vegetable oil-based organogels and bigels

Organogels are widely used as delivery platforms for active ingredients (transdermal, oral, and parenteral routes), self-healing materials for pharmaceutical, nutraceutical, and cosmetic industries [90,91]. Organogels [92] are considered as viscoelastic systems composed of a constant liquid phase (normally an organic solvent), a mineral or vegetable oil, all of them immobilized in a three-dimensional network [91]. Vegetable oils, including sunflower, corn, sweet almond, cod liver oil, and olive oil has been widely used as the liquid phase of the system due to their antioxidant, nutritional characteristics, and long shelf-life. Ideal characteristics that make them attractive to prepare oral and cosmetic formulations. Olive [93], sesame [94], and castor oil [95] based organogels for controlled drug delivery for topical/transdermal applications were developed in the last years. Besides its health benefits, the advantages of using VOs are its green nature, a trend in natural cosmetics, and its influence on the gelation and solubility properties of the organogels [96]. However, organogels present some limitations: their limited large-scale production [90], and toxicity of some organic solvents that can constrain their biomedical applications. These drawbacks were overcome by the developments of bigels [90]. They are described as a system that combines a mixture of a hydrogel (aqueous phase) and organogel (oil phase), resulting in exciting thermal, rheological, structural, and electrical properties [92]. Bigels advantages include delivery of hydrophilic and hydrophobic molecules, cooling, and moisturizing effect, spreadability, and facilitated synthesis. Sunflower, sesame, almond, and olive oil were used for bigels synthesis for drug delivery applications and cosmetics [92]. There is evidence that bigels with superior mechanical properties display a lower drug release rate [92]. Therefore, further investigation is required to prepare a system with better properties together with an enhanced drug release rate. Bigels obtained by mixing guar gum hydrogel and sorbitan monostearate sesame oil-based organogel were produced. The system showed improved biocompatibility with drug (ciprofloxacin) loaded bigels exhibiting interesting antimicrobial activity against *Bacillus subtilis* and opening their application for topical delivery of antimicrobials [97]. Sesame oil was used to synthesize biocompatible and antimicrobial (*E. coli*) bigels for topical delivery of drugs for bacterial vaginosis [98]. Although bigel systems are not commercially available, literature evidences their potential application as carriers for the controlled release of active substances for topical and transdermal applications.

4. Prospects for the synthesis of vegetable oils derived biomaterials for biomedical engineering applications

It is widely reported that healthy tissues and organs maintain a controlled balance between oxidants and antioxidants molecules. Oxidants are characterized by reactive oxygen species (ROS) production that comprises a family of molecules (hydrogen peroxide, hydrogen radicals, hydroxyl ions, superoxide anions, nitric oxide, peroxynitrates, and hypochlorite, including others). Interestingly to restore the redox equilibrium, every cell is equipped with multiple endogenous antioxidant systems, including the glutathione and thioredoxin system, vitamins, and protective enzymes [99,100]. The disruption of the equilibrium between oxidants and antioxidants is defined as oxidative stress, which can be a result of several internal and external physiological processes where biomaterials implantation is included. In the physiological environment, biomaterials' physicochemical properties contribute to oxidative stress through the constant oxidative attack by immune cells and the release of degradation products that can result in ROS overproduction [38,100,101]. Resuming, ROS generation is one of the existing problems during biomaterial implantation, degradation, and tissue regeneration [102,103]. Therefore, developing scaffolds with antioxidant capability for tissue replacement to protect against the harmful effect of free radicals is mandatory [104]. The current approach to managing oxidative stress in biomaterials science is to incorporate antioxidants molecules into scaffolds for therapeutic liberation by diffusion and/or degradation sustaining the redox balance [105–109]. Biomaterials with radical scavengers comprising ascorbic acid, ferulic acid, or antioxidant enzymes were already reported and have been shown to diminish oxidative stress, improving cell survival [110]. We can foresee an opportunity in this field to propose using VOs (see Fig. 4) with its intrinsic antioxidant molecules conjugating them with polymeric scaffolds. A possible successful strategy that enables ROS reduction and modulates cell behavior. A more elegant approach can be the development of smart polymeric biomaterials sensitive to oxidative stress. They might sense oxidative stress releasing bioactive antioxidants molecules in response to the oxidant concentrations. They are known as ROS-responsive biomaterials that can be in the form of nanoparticles (for drug delivery systems), as well as hydrogels, able to reply to physiological oxidative stress, protecting cells and tissues. ROS-responsive polymers can be degraded in situ to discharge antioxidant molecules in response to local ROS accumulation, and literature already reviews their applications as drug delivery agents, prodrugs to control tissue microenvironments endorsing tissue regeneration and cancer therapy [105–109]. Although the applications of ROS-responsive biomaterials in TE are still in their infancy and are far from clinical translation, they are considered a new trend where vegetable oils might play an important role. Another concern upon biomaterials implantation, independent of the class of materials, is the complex cascade of inflammatory signals that are orchestrated with the main goal of clearing damaged cells, eliminating pathogens, and even restoring tissue homeostasis [104]. This inflammatory response is characterized by ROS, inflammatory molecules, proteases, and antimicrobial sub-stances release, that depending on their concentration can instigate tissue damage and/or can help in tissue regeneration [102,103]. So, a perfect balance between oxidants and antioxidants is mandatory since ROS work as a chemo-attractants that activates important signaling pathways involved in the orchestration of inflammation, healing, and regeneration [107]. Prolonged and excessive ROS levels in many cases induce propagation of inflammation, fibrous encapsulation, insufficient angiogenesis, necrosis, compromising biomaterial's biocompatibility and function [103,111]. Concerning inflammation, the tendency is to target inflammatory and immunomodulatory pathways working with biomaterials properties (chemistries, stiffness, porosity, topography, size, and shape) to mitigate unfavorable foreign body reactions.

However, advanced strategies try to manage inflammation and oxidative stress during biomaterial implantation to improve their integration [102,103]. To accomplish that, materials can be designed to direct and program a specific host response, where anti-inflammatory and antioxidant molecules can be incorporated and released over time. It is conceivable that grape, sesame, and olive oil with their intrinsic anti-inflammatory and antioxidant properties can be used to design novel polymeric scaffolds that locally deliver anti-inflammatory moieties and/or scavenge ROS from injured tissue sites. Possibly they can be designed to activate synergistic pathways involved in host response and tissue regeneration. Besides oxidative stress and inflammation, most of the biomaterials fail as a result of infections. The combined action of inflammatory inhibitors and antibiotics into biomaterials has been used as a methodology to reduce infection after surgery. However, the long-term use and the employment of conventional antibiotics have promoted antibiotic resistance development. An emerging promising approach to avoid infection is the use of antibiotic-

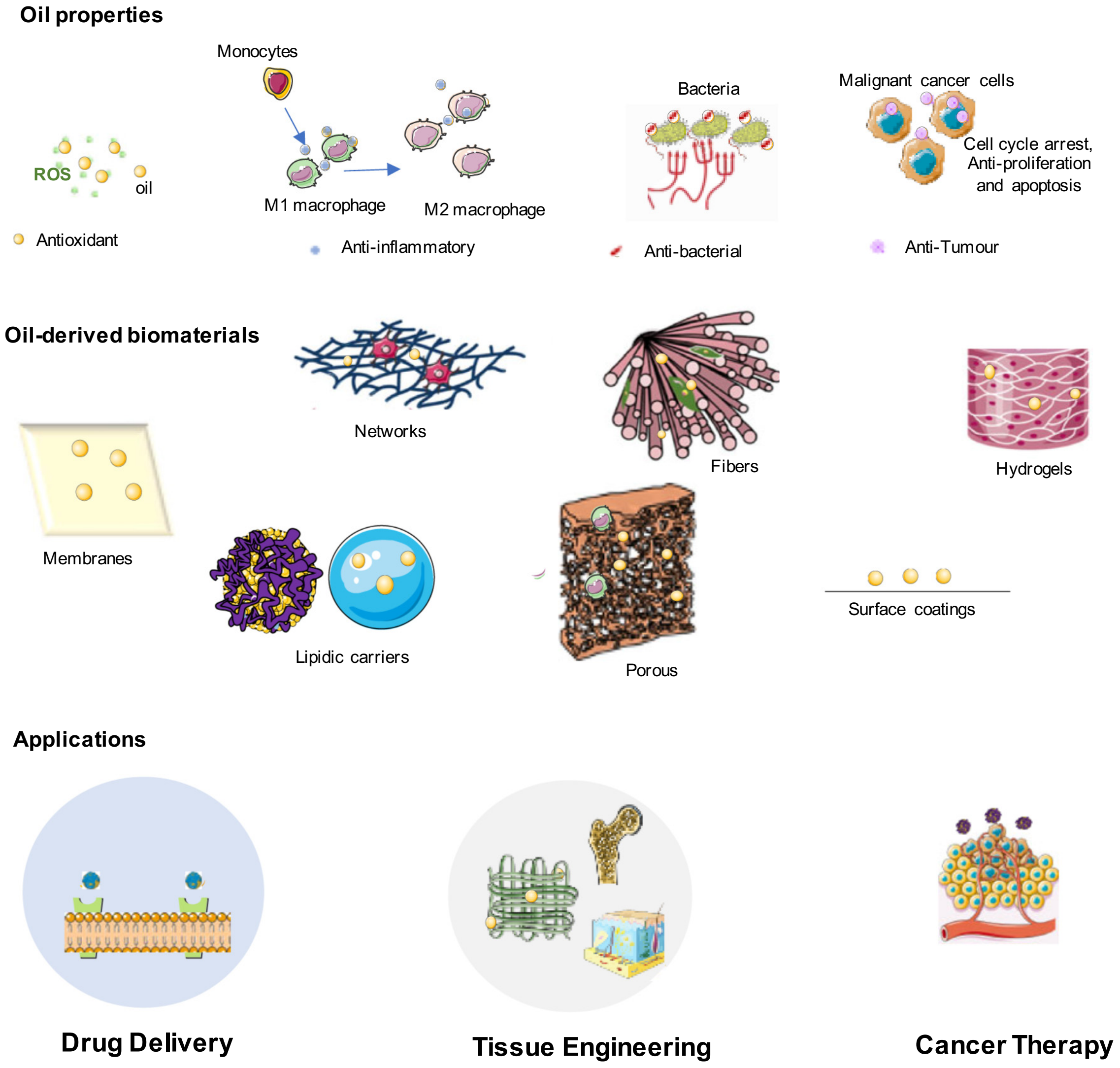

Fig. 4. Possible vegetable oil-derived biomaterials: Plant oil has in its constitution antioxidant, anti-inflammatory, antibacterial, and antitumor molecules. Full oil composition or isolated oil biomolecules can be assembled with membranes, networks, fibrous, hydrogels, particles, coatings, porous structures and applied in drug delivery, bone, and skin tissue engineering, and cancer therapy applications.

free strategies. By taking advantage of the chemistry and structure of olive, grape, and castor oil capability to intrinsically kill pathogens, it is possible to envisage their use in antibacterial scaffolds. Therefore, novel approaches to prevent and kill bacteria, modulate inflammation, and reduce oxidative stress are demanded. Recently the use of scaffolds as delivery systems of anti-inflammatory, antioxidant, and antibacterial molecules seems to be an interesting approach for tissue engineering and regenerative medicine area, where VOs can play an important role [24,112]. Biodegradable fibrous, films, hydrogels, and particles scaffolds (see Fig. 4) seem to be attractive carriers that retain the long-term stability of vegetable oil cargo without oxidation, enabling their controlled release and consequent therapeutic stability and effectiveness. Still, there is the need to understand the perfect amount of each bioactive oil molecule, their bioavailability within the scaffold, and the consequent health benefits associated with such a system. The possible application of the referred systems will be discussed below.

4.1. Skin tissue engineering and bio-cosmeceutical formulations with photoprotection

More than 11 million and 6.5 million people are affected by burn injuries and chronic wounds every year. Most of the efforts have been made to develop antibiotic-loaded wound dressings that are already commercially available; however, they are always limited to a tight range of bacteria. It is possible that the use of grape, castor, and olive VOs compounds with their wide range of antibacterial (*E. coli*, *S. aureus*, *L. acidophilus*, *L. acidophilus*, *B. bifidum*, *H. pylori*, and *S. enteritidis*) properties may provide solutions to overcome this problem. Chronic wounds are also a complication in patients with diabetes mellitus that can lead to foot ulcers and consequent amputation. These patients are prone to oxidative stress and inflammatory-related pathologies with consequent excessive production of ROS [109]. The extreme ROS generation and its ineffective and time-consuming removal at the injury site com-promise ECM structure and functions compromise healing [107,108]. Skin TE has been using nanofibrous, membranes, hydrogels, injectable gels, nano/microspheres scaffolds of natural and synthetic polymers combined or not with cells that improve healing and skin tissue regeneration [113]. The development of bioactive and pro-regenerative scaffolds with specific biomolecules that locally reduce oxidative stress and modulate immune function (triggering and recapitulating key natural healing cascade events) is a new concept in the field, where grape, soybean, and olive VOs can play an important role. As the immune response is also dependent on the 3D microenvironment, we consider that the combination of the antimicrobial, antioxidant, and anti-inflammatory properties of grape and olive oil in a 3D polymeric matrix can be a strategy to develop pro-regenerative scaffolds that thereby will avoid infection, steer host's immune system and possibly achieve skin natural healing response [113]. The biomedical significance of oil-based organogels and bigels is newer, and the fact that depending on their physicochemical characteristics, they can display useful properties such as thermoreversibility, thermostability, and photoresponse can allow their application in skin TE. Vegetable oils have been suggested as photo-stability enhancers, friendly carriers offering hydration to the sun-unprotected skin, exhibiting a sun protector factor [114]. For example, literature already reveals that olive and coconut oil sun protector factor was higher than castor and almond oil, highlighting the capacity of these oils as UV-filters [114, 115]. Their photo-stability associated with peculiar redox features and chelating metal characteristics makes them excellent free radical scavengers that inhibit, and repair photo-oxidative stress provided by solar radiation [114]. So far, no natural UV filter has been approved in the EU market. It is possible that the encapsulation of vegetable oil or specific oil biomolecules (sesamol from sesame, proanthocyanidins from grape, and tocopherols from soybean) into carriers could be a favorable strategy to formulate sunscreen products with a lower organic UV-filter content. Taking the benefits of grape and sesame oil properties, they can be used to design new advanced bio-cosmeceutical which the synergy interplay of oil UV filters, antioxidant and anti-inflammatory properties will be able to enhance sunscreen efficacy by boosting the skin endogenous defense from UV-driven inflammation.

4.2. Bone and cartilage tissue engineering

Oxidative stress is associated with the development of bone diseases, such as rheumatoid arthritis, which contributes to increased mortality rates observed worldwide. In vitro and in vivo data reveal that olive oil polyphenols and soybean oil flavonoids (genistein and daidzein) have gained interest due to their ability to promote osteoblastogenesis, with some compounds preventing bone resorption and arthritic damage through their anti-inflammatory and antioxidant properties [116]. As in osteoarthritis, there is an increase in ROS several antioxidants' molecules such as vitamin C and E, polysaccharides, and/or polymers with specific drugs has been used [107]. For example, synthetic resveratrol (a compound naturally present in grape oils) encapsulated in PLGA nanoparticles reduced the secretion of pro-inflammatory agents (IL-6 and TNF-α) and increased the expression of anti-inflammatory genes, including (IL-10 and vascular endothelial growth factor (VEGF)), which promoted osteogenesis [103]. In another study, the effect of resveratrol decreased cartilage damage and inflammation, suggesting the potential of resveratrol as a natural anti-inflammatory molecule that enhances cartilage and tissue regeneration [103,117,118]. Further studies are necessary to clarify the mechanism of action and the dose of resveratrol necessary for modulating inflammation in clinical applications; however, it seems to be a candidate for bone tissue engineering. We believe that natural polymeric (collagen/gelatin, alginate, chitosan, silk, hyaluronic acid, elastin, glycosaminoglycans, peptides, etc.) and composite scaffolds along with natural resveratrol from grape seed oil be used in bone and cartilage tissue engineering. Due to bioavailability and solubility limitations, it is essential to maintain the chosen concentration of biomolecule at the target site, so strategies to encapsulate oil bioactive molecules into scaffolds for local delivery should be developed to ensure an efficient method and a constant supply at the implant site [116].

4.3. Vegetable oils biomolecules as new anticancer agents

There were an estimated 18.1 million new cases of cancer with 9.6 million deaths worldwide in 2018. It is the leading cause of death, with breast, lung, prostate, colon, and skin cancers presenting a higher incidence and prospects to increase in the next two decades [119]. Cancer treatment commonly involves surgeries followed by radiation therapy and chemotherapy. The literature already reported that 50% of the conventional chemotherapy agents are derived from plants, with 25% being chemically modified versions of phytoproducts. New therapies have been accepted in the last years, with natural anticancer molecules (e.g., vinca alkaloids, semi-synthetic epipodophyllotoxins, taxanes, and camptothecin) approved by FDA. Curcumin, resveratrol, isoflavone, lycopene, and phytosterol are also understudy with the main goal of work as adjuvant [119]. So, proposing specific vegetable oils biomolecules as a new anticancer agent can be an interesting approach. There is already experimental evidence suggesting that proanthocyanidins, resveratrol, vitamin E and phenolic compound of grape seed oil, isoflavones of soybean oil, sesamin, and sesamol from sesame oil are responsible for their anti-cancer activities [120,121]. Hence, it can be potentially employed as a successful therapeutic adjuvant molecule to prevent and treat cancer development and progression [122,123]. As literature associates high levels of ROS with aberrant cancer cell growth, it is possible that the antioxidant properties of the oils can be a promised strategy to treat cancer cells with minimal side effects. Grape, soybean, sesame, and olive oil antioxidant properties may play a chemopreventive role, but also can be exploited as potential anticancer substances that alone or combined with other chemotherapeutic agents or drugs can be potentially exploited for cancer therapy. Grape, soybean, sesame, and olive oil can play an important role in the post-surgery management of patients who have undergone surgical removal of solid tumors. Normally local chemotherapy with the administration of anticancer drugs can minimize the possibility of recurrence of the disease. In last year's several implantable biomaterial scaffolds [50,124–126] (e.g., hydrogels, particle-based system, coatings) have been highly considered appropriate since they protect the locally injected drugs, prolonging their retention time [126,127]. For small and/or inaccessible tumors, nanoparticle and microparticle biomaterials with antitumor encapsulated drugs have been developed. Alternatively, hydrogels and cryogels seem to be another surgery-free system with a 3D environment, where a controlled spatial and temporal drug delivery is possibly achieved. It is possible that vegetable oils with their intrinsic antitumor and chemopreventive properties can play an important role. To improve drug absorbance and encapsulating efficiency, vegetable oils organogels, and bigels can also be used. Although most available studies are in their infancy, the knowledge of the mechanisms of action in a manner that facilitates clinical applications is mandatory to improve their translatable efficacy.

5. Conclusions

This review provides a quite promising future of vegetable oils in biomedical applications. Vegetable oils are highly abundant and sustainable bioresources found in nature, with low price and biodegradability as well as they present enhanced biocompatibility. VOs alone are limited by their physiochemical properties, degradation, structural heterogeneity. Their heterogeneity and stability of its composition are dependent on the region in which the plant is grown, agricultural techniques used to cultivate, the maturity of the fruit at harvest, and sometimes the processing technique. To overcome this limitation, vegetables can be easily grown using good agricultural practices and under controlled environments, resulting in a well-controlled oil. Also, chemical modification of oil biomolecules or their integration with natural and/or synthetic materials with superior chemical stability and mechanical properties can be an interesting approach for biomedical applications. However, alone they do not provide all the biomedical desired properties, and then their integration in biomaterials must act in synergism to achieve the necessary biological performances of the resulting biomaterials. Still, there is a need for a comprehensive understanding of vegetable oil bioactive molecules and the processing methods for successful clinical product development. Through physical or chemical bioconjugation, scientists have developed many techniques and procedures to incorporate oil biomolecules into biomaterials, transforming them to suit the intended bio-material application. We propose the use of the combination of natural polymers with specific moieties of VOs to develop ROS-responsive, anti-inflammatory, and antibacterial scaffolds for biomedical applications. Notwithstanding the vast evidence in support of oil-derived biomaterials as an inherently safe biomaterial, further research may be required to characterize their toxicology, and immunogenicity needs to be elucidated comprehensively. Future research can address the current degree to which these bioactive molecules are bioavailable, absorbed, metabolized, distributed, their toxicity, and health issues such as elimination by the human body should be done, comprehensively. We believe that using oil FDA-approved molecules to build new polymeric materials can reduce the regulatory burden, however with the increase of design complexity, manufacturing costs, and regulatory procedures to demonstrate safety and efficacy increase as well. We believe that vegetable oil-derived materials can revolutionize fields of tissue engineering or regenerative medicine.

CRediT authorship contribution statement

The manuscript was written by Ana R. Ribeiro and all the other authors corrected the draft and give their contributions. All authors have approved the final version of the manuscript.

Declaration of competing interest

There are no conflicts to declare.

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