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Review

Valorization of Tomato Residues by Supercritical Fluid Extraction

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Abstract: Tomato processing leads to the production of considerable amounts of residues, mainly in the form of tomato skins, seeds and vascular tissues, which still contain bioactive molecules of interest for food, pharmaceutical and nutraceutical industries. These include carotenoids, such as lycopene and β-carotene, tocopherols and sitosterols, among others. Supercritical fluid extraction is well positioned for the valorization of tomato residues prior to disposal, because it remains an environmentally safe extraction process, especially when using carbon dioxide as the solvent. In this article, we provide an extensive literature overview of the research on the supercritical fluid extraction of tomato residues. We start by identifying the most relevant extractables present in tomatoes (e.g., lycopene) and their main bioactivities. Then, the main aspects affecting the extraction performance are covered, starting with the differences between tomato matrixes (e.g., seeds, skins and pulp) and possible pretreatments to enhance extraction (e.g., milling, drying and enzymatic digestion). Finally, the effects of extraction conditions, such as pressure, temperature, cosolvent, flow rate and time, are discussed.

Keywords: biomass; carotenoids; supercritical fluid extraction; tocopherols

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1. Introduction

Tomato is a key ingredient in many diets worldwide, and is associated with several health benefits, mainly attributed to the presence of carotenoids such as lycopene; it exhibits antioxidant activity and prevents cardiovascular and other diseases [1]. Even though some tomatoes are consumed fresh, the majority are transformed into a multiplicity of processed products. The production of tomatoes keeps increasing every year, with a gross value estimated at USD 90 billion in 2019 [2], as does the waste generated, such as pomace, seeds, skins, juices and pastes, which can represent up to 40% of the raw material [3]. Currently, these wastes are dumped into landfill or reused for animal feed, even though their composition potentiates other applications such as the extraction of nutrients and bioactive compounds for food, pharmaceutical and nutraceutical products. Moreover, ripe tomatoes are the most abundant source of lycopene, 90% of which is located in the skin [4], which constitutes the greater part of the wastes [4]. In this sense, the valorization of tomato processing byproducts is a biorefinery challenge that can provide a natural source of valuable carotenoids and other added-value compounds.

The extraction of vegetable materials is conventionally performed with organic solvents. However, their toxicity for humans and the environment can be a major impediment for food, pharmaceutical and cosmetic applications, as well as at the economic level, because its use is increasingly regulated with expensive waste treatment procedures. Under the principles of green chemistry, processes should prevent waste production and reduce the use of solvents and hazardous chemicals to become safer and more energy efficient [5]. Following these guidelines, research has focused on developing the potential of greener processes and solvents such as the use of microwaves, ultrasounds, pressurized solvents, green solvents, enzymatic pretreatments and bio-solvents [6]. Microwave-assisted extraction (MAE) uses microwave radiation to rapidly increase the temperature and pressure

inside the vegetable cells, causing their expansion and disruption, and releasing the contents, which improves the extraction performance. This method provides faster extractions, reducing the energy cost and the volume of necessary solvent [7,8]. However, the high temperatures achieved can degrade thermolabile carotenoids such as lycopene. The valorization of tomato residues with MAE has been reported for the extraction of phenolics, flavonoids and carotenoids [9–12]. Ultrasound-assisted extraction (UAE) is another alternative method which utilizes ultrasound instead of radiation. Acoustic cavitation is generated in the cells, bursting them, and improving mass transfer. Additionally, mild temperatures are easier to maintain, reducing the risk of compound degradation. The UAE of pectin and carotenoids, especially lycopene, from tomatoes has been reported [13–17]. A distinct method, which relies on the pretreatment of the biomass with enzymes, is enzyme-assisted extraction (EAE). In this case, the biomass is exposed to enzymes which degrade the cell walls and membranes, and thus facilitate the release of bioactive compounds during extraction. Lycopene EAE from tomatoes was reported as successful by several authors [18,19], although technical limitations due the high cost of enzymes and different efficiencies depending on the conditions can compromise its scaling-up [7]. High pressures are also effective in the disruption of cells and membranes, forming the basis of pressurized liquid extraction (PLE) and high hydrostatic pressure extraction (HHP), improving the recovery of lycopene from tomato wastes [20,21]. The combination of previous techniques has also been reported for tomato waste valorization, specifically UAE and MAE [22], EAE and UAE [23], and EAE and high pressures [19]. Even though these alternative methods reduce the volume of solvents utilized, the extraction time and the energy cost, with improvements on the extraction performance, they still rely on the use of organic solvents such as *n*-hexane, ethyl acetate, acetonitrile, chloroform, ethanol, acetone and petroleum ether. However, greener solvents can be obtained from renewable sources, such as *d*-limonene from orange peel. This bio-solvent has been applied for the recovery of carotenoids from tomato, showing no significant differences from conventional dichloromethane extraction [24]. Due to the insolubility of carotenoids in water, it is not a common solvent for tomato waste valorization.

Supercritical fluid extraction (SFE) addresses these concerns, especially when using CO_2, providing a versatile solvent that can be tuned according to the properties of the target compounds and, simultaneously, an environmentally innocuous separation from the extracted solutes. Even though solvents such as supercritical ethane have been tested, supercritical CO_2 remains the most successful choice due to its low critical point (73.8 bar and 31.0 °C) [25], enabling the extraction of thermolabile compounds (such as carotenoids), as well as benefits due to its availability, low price, non-toxicity and safety [6,26]. The manipulation of pressure and temperature significantly impacts the supercritical solvent density, viscosity, diffusivity and solubility parameters, easing the penetration of porous matrices, the enhancement of mass transfer, as well as enabling the fine-tuning of the solvating power of supercritical carbon dioxide (SC-CO_2), which is essential during extraction and for separation of the obtained extracts by depressurization.

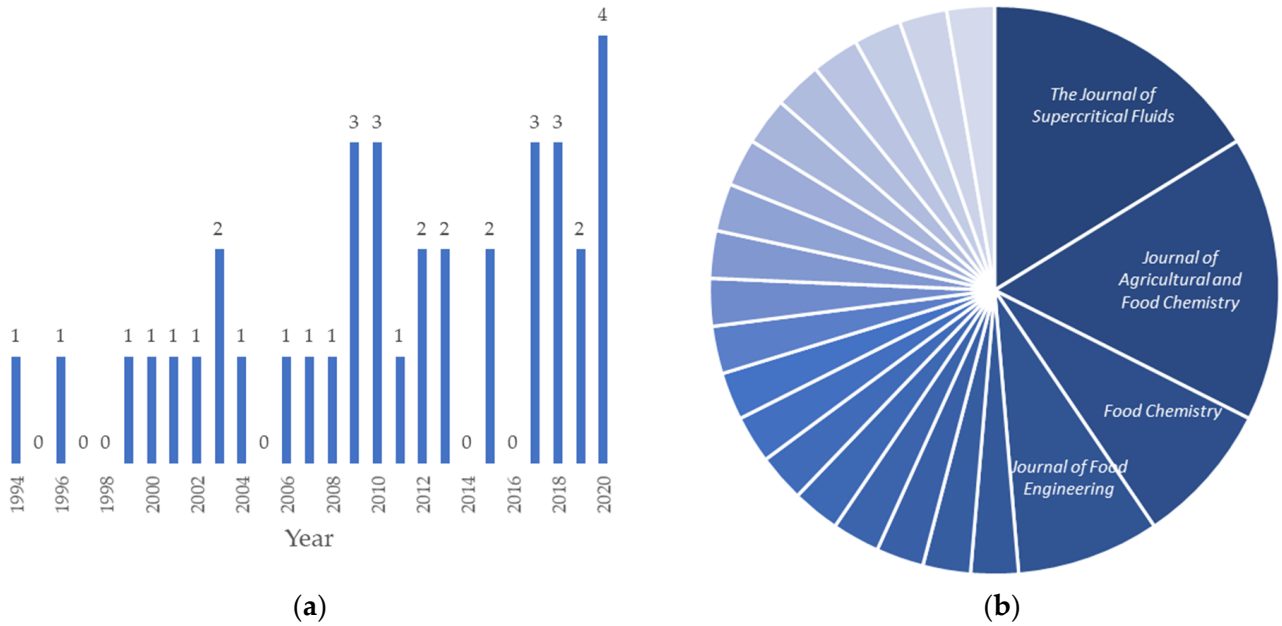
Multiple SFE processes have been proposed; for instance, for the extraction of oil and diterpenes from spent coffee grounds [27], sterols from water hyacinth [28], phenolic compounds and anthocyanins from juçara residues [29], astaxanthin and lutein from microalga [30], phenolic compounds from cacao pod husk [31], friedelin from oak tree cork [32], lupeol and β-amyrin from grape vine leaves [33], triterpenic acids from eucalyptus leaves [34], triterpenoids from acacia leaves [35], and ginsenosides from ginseng roots [36]. Melo et al. provide an extensive review covering several other vegetable matrices [37].

Research on tomato waste valorization using SFE started in the 1990s and has slowly increased until today. Several reviews on this topic have focused on lycopene recovery [26], specific morphological parts or residues [38–40], the different extraction methods [7], and possible valorization routes [41]. This paper provides an overview of the literature on the SFE of tomato processing residues, aiming to cover the main molecules of interest, the

type of tomato residues used, the employment of pretreatments and the influence of the SFE operating conditions on the contents of extractives and its potential for biorefinery processes for food, pharmaceutical and cosmetic industries. Additional data have been measured to enrich the discussion.

2. Literature Overview

The supercritical fluid extraction of tomato is well reported in the literature, with over thirty-five articles focusing on this topic. Since the 1990s, there has been about one article per year on tomato SFE, with an increase in publications in the last decade (see Figure 1a). From Figure 1b, one may see that there is a large distribution of these articles over several journals, with nineteen journals with only one publication. Nevertheless, *The Journal of Supercritical Fluids* and the *Journal of Agricultural and Food Chemistry* can be identified as preferred journals for this topic.



(**a**) (**b**)

Figure 1. Number of studies studying the supercritical fluid extraction of tomato through the years (**a**) and the most common journals where they appear (**b**). Search was performed in Scopus using the keywords "supercritical extraction tomato".

From the SFE publications available, 70% performed a kinetic study, evaluating the extraction rate over time. SFE studies tend to be very experimental, with only 16% providing some sort of modeling approach. This can be the modeling of extraction curves, using the Sovová model [42,43] or the Brunner equation [44], or modeling the solubility of the target compounds in the supercritical fluid, often using the Chrastil model [45]. About 19% take a design of experiments (DoE) approach to define experimental runs and conditions.

Most SFE processes use supercritical CO_2 as a solvent, mainly because it is inert, non-toxic, non-flammable, non-explosive, and possesses null interfacial tension and an easy-to-reach critical point. SFE of tomato is no exception to this, with ethane being tested in one study [46]. The supercritical fluid (SCF) is employed without any cosolvent in most publications (84%). The remaining studies use ethanol [47–49], water [49], vegetable oil [50], canola oil [49], avocado oil [51] or hazelnut oil [52] as cosolvents.

The most relevant operating conditions in SFE processes are pressure, temperature and the solvent flow rate per mass of biomass (e.g., tomato). A wide range of pressures have been explored, from 77 bar, a point close to the critical pressure of CO_2, to 550 bar, a common maximum threshold for SFE equipment. In terms of temperature, conditions ranged from 32 °C, once again, close to the critical temperature of CO_2, to 110 °C (the usual temperature

limit of SFE units is around 100 °C). A comparison of flow rates between published research is more difficult to accomplish because no systematic reporting is performed. Some authors report the volumetric flow rate, whereas others report the mass flow rate; some do not report other valuable information such as the mass of material, extractor dimensions, or extraction time. Available data indicate that flow rates from 0.01 to 400 kg_{SCF} kg^{-1} have been utilized or, for those reported in volumetric terms, from 0.05 to 400 L_{SCF} kg^{-1}. For reference, extraction times ranged from 10 min to 8 h.

SFE equipment can currently be acquired from many companies offering turn-key solutions of benchtop, pilot and even production-scale units. Most research has been performed using equipment from Supercritical Fluid Technologies, Inc. (Newark, DE, USA), Applied Separations (Allentown, PA, USA), and Separeco (Pinerolo, Italy), which appear to be the most common contemporary suppliers.

Table 1 lists all published research involving the SFE of tomato biomass and summarizes the main operating conditions (pressure, temperature, SCF flow rate, cosolvent uses (if any) and extraction time), as well as other relevant information such as the tomato source, pre-treatment applied prior to extraction and target extracts. This list encompasses all results for a Scopus search of articles containing the words "supercritical extraction tomato" in the title, where experimental extraction studies are conducted.

In addition to extraction studies of tomato, there are characterization studies of tomato parts or extracts [53–56], solubility studies of extractable compounds [57,58] and an economic analysis of the SFE process [59].

Table 1. Summarized information on scientific articles dealing with the SFE of tomato. Scopus search for articles containing the words "supercritical extraction tomato" in the title as of July 2021. The supercritical fluid (SCF) is CO_2 unless otherwise specified. Articles are ordered by ascending year of publication.

Tomato Part	Pre-Treatment	Particle Size	Cosolvent	Pressure (Bar)	Temperature (°C)	SCF	SFE System (Model, Company)	Targets	Best Yield or Recovery	Ref.
seeds	dried, milled, sieved	0.25–0.46 mm	No	245	40	50–392 kg/kg_{bio}	-	oil	0.4 kg/kg oil free sample	[60]
seeds	dried, milled	0.27 mm	No	108–245	40–70	295 kg/kg_{bio}	-	oil	0.3 kg/kg sample	[61]
pulp or skins of ripe tomatoes	dried, ground	-	No	172–275	40–80	6000 L/kg_{bio}	SFE-400, Supelco	lycopene and β-carotene	64.41 (lyc) mg/100 g 34.88 (beta) mg/100 g	[62]
paste waste	dried, ground, sieved	3 mm	5–15% EtOH	200–300	35–65	33–400 kg/kg_{bio}	Extraction setup, Sitec Sieber	lycopene and β-carotene	51% (lyc) 50% (beta)	[47]
skins	dried, powdered	-	No	400	60–110	400 L/kg_{bio}	SFX-3560, Isco	lycopene	100%	[63]
seeds and skins	none	-	No	138–483	32–86	16–100 L/kg_{bio}	SFX-210, Isco	lycopene and tocopherols	7.19 ug/g, 61% (lyc), 0.15 ug/g, 86% (toc)	[64]
skin and pulp	dried, ground	-	No	77–281	40	240 L/kg_{bio}	7680A, Hewlett-Packard	all-trans-lycopene	88% (% of total lyc)	[65]
seeds and skins	dried, ground	80 and 345 μm	No	250–300	60–80	120 kg/kg_{bio}	TOC-27-40, HIP	lycopene and β-carotene	80% (lyc), 88% (beta)	[66]
sun-dried tomato	dried, ground	1 mm	1–20% vegetable oil	335–450	45–70	15–53 kg/kg_{bio}	-	lycopene	60%	[50]
skins	dried	-	No	200–500	40–100	1.5–4.5 mL/min; 330 min [d]	10 mL, Thar Designs	lycopene	1.18 mg/g (lyc)	[67]

Table 1. *Cont.*

Tomato Part	Pre-Treatment	Particle Size	Cosolvent	Pressure (Bar)	Temperature (°C)	SCF	SFE System (Model, Company)	Targets	Best Yield or Recovery	Ref.
pomace	none	0.3–0.6	No	380–460	40–80	0.05 L/kg_{bio} [c]	-	carotenes and tocopherols	9.04 mg/g (carotenoids), 5.96 mg/g (tocopherols)	[68]
skin and seeds	ground, pre-treatment with modifier		5–15% EtOH	250–450	40–70	29,167 L/kg_{bio} [c]	Spe-ed SFE NP 7013,Applied Separations	lycopene	23.9 ug/g (lyc)	[48]
pulp and skins	dried, ground, mixed with hazelnuts	1 mm	No	400–450	60–70	21–53 kg/kg_{bio}	-	lycopene	72.5%	[69]
skins	freeze-dried, ground	1 mm	5–15% EtOH, water, canola oil	250–350	45–75	3.5 L/min [d]	Spe-ed SFE NP 7013,Applied Separations	lycopene	73.3% (lyc) (49:3 *trans*:*cis*)	[49]
skins and seeds	dried, ground	0.15–0.72 mm	No	200–300	40–80	0.01–0.07 kg/h [d]	-	trans-lycopene	93% (lyc)	[70]
seeds	dried, ground, mixed with grape seeds		No	335–450	45–70	21–53 kg/kg_{bio}	-	oleoresins	-	[71]
juice	removed serum	-	No	200–350	40–80	0.01–0.04 kg/kg_{bio}	-	lycopene	76.9%	[72]
ripe tomato puree	dried, processed to puree	-	No	450	65–70	41–46 kg/kg_{bio}	-	lycopene	80% 9.31 mg/g	[73]
pomace	freeze-dried, powdered	0.2–0.45 mm	No	350–450	40–60	[d]	SFX-220, Isco	lycopene	32.5 g/100 g dw	[74]

Table 1. *Cont.*

Tomato Part	Pre-Treatment	Particle Size	Cosolvent	Pressure (Bar)	Temperature (°C)	SCF	SFE System (Model, Company)	Targets	Best Yield or Recovery	Ref.
peel and seed	ground, sieved	1 mm	No	200–400	70–90	90–180 L/kg_{bio}	10 mL vessel, Thar Tech	lycopene and β-carotene	56% (lyc), 68% (beta)	[3]
skins and seeds	dried, ground	0.15–0.56 mm	No	120–300	40–80	19–131 kg/kg_{bio} [a]	-	lycopene	80%	[46]
pomace and byproducts of SFE	freeze-dried, milled	500 µm	No	450	65–70	41–46 kg/kg_{bio}	-	carbohydrate	-	[75]
pomace	wet	-	No	100–300	30–50	5–15 kg/h [d]	Pilot plant, Muller Extract	lycopene	1.58 mg/L	[76]
pomace	dried, ground	-	No	69–275	40–80	9.6–28.8 L/kg_{bio}	SFT-100, SupercritiCalFluid Technologies	lycopene	82%	[77]
ripe tomato puree	freeze-dried, puree, enzyme digestion	1 mm	No	500	86	10 L/kg_{bio} [c]	Spe-ed SFE, Applied Separations	lycopene	27.6 mg/g dw	[78]
pomace	freeze dried, milled, mixed with avocado		avocado oil [b]	200–400	40–60	71 kg/kg_{bio}	-	lycopene	80%	[51]
pomace	sun-dried, ground	300 µm	No	300–500	50–80	31–63 kg/kg_{bio}	Spe-ed SFE-2/4,Applied Separations	lycopene and β-carotene	60.8% (lyc), 58.8% (beta)	[79]
pomace	freeze-dried, ground	-	No	200–550	40–80	[d]	SFT-150, SupercritiCalFluid Technologies	*cis*-lycopene	62% of total lyc (*cis*-lyc) 251.15 g/kg dw (oleoresin)	[80]

Table 1. *Cont.*

Tomato Part	Pre-Treatment	Particle Size	Cosolvent	Pressure (Bar)	Temperature (°C)	SCF	SFE System (Model, Company)	Targets	Best Yield or Recovery	Ref.
puree	dried, sieved	-	No	350	60	4.8 L/kg_{bio}	Spe-ed SFE, Applied Separations	lycopene and β-carotene	2.92 g/kg (all-trans-lyc), 1.12 g/kg (beta)	[81]
pulp	dried	0.25 mm	5% hazelnut oil	300–500	50–80	225 L/kg_{bio}	10 mL vessel, Thar Tech	lycopene	22%	[52]
peel and seed	dried, milled	0.1/1 mm	No	300–500	40–80	12 L/kg_{bio}	SFT 110, Supercritical Fluids	lycopene	246 g/kg (oleoresin)	[82]
peel and seed	dried, milled	-	No	400	60	20 L/kg_{bio}	SFT 110, Supercritical Fluids	lycopene	1.32 mg/kg	[83]
skin	dried	350 µm	No	350–550	60	2.2 L/kg_{bio}	Spe-ed SFE, Applied Separations	lycopene and β-carotene	79% (oil) 0.86 (lyc), 1.5 (beta) mg/100 g	[84]
pomace	wet	-	No	380	80	100 kg/kg_{bio}	Separeco	lycopene	619 mg/kg (lyc)	[85]
powder	freeze-dried, ground	-	No	400	50	10.8–18 kg/kg_{bio}	-	high antioxidant activity	3.91 g/100 g dw (total), 64.9% (lyc), 34.9% (beta)	[86]
pomace	dried, milled or powdered	0.2–1.5 mm	No	380	80	35 kg/kg_{bio}	Separeco	lycopene	165.3 g/kg (total), 1.34 mg/g (lyc)	[87]
peels	dried, ground	-	No	400	70–80	300 kg/kg_{bio}	Natex	lycopene and β-carotene	39.1 mg/g dw (lyc), 68.2 mg/g dw (beta)	[88]
pomace	dried	As is	EtOH and EtAc	300	60	216 kg/kg_{bio}	Spe-ed SFE Helix, Applied Separations	oil	30.56 g/kg	Unpublished (see S.M.)

[a] Ethane as the supercritical fluid; [b] avocado oil functions as cosolvent; [c] static and dynamic extraction; [d] Not enough data to report SCF usage in kg_{SCF}/kg_{bio}; pomace: skins, seeds, and vascular tissues; puree: pulp with no seeds, skins or tissues; EtOH: ethanol; EtAc: ethyl acetate; lyc: lycopene; beta: β-carotene; toc-tocopherols; dw: dry weight; S.M.: Supplementary Materials.

3. Target Compounds

The valorization of tomato residues by SFE usually aims to produce extracts rich in one or various carotenoids (lycopene and β-carotene) and/or tocopherols (α-, γ- and δ-tocopherol). Lycopene is by far the most sought-after compound in tomato residues, with nearly all studies exploring its recovery from the tomato matrix. From the studies dealing with the SFE of tomato materials, listed in Table 1, about 84% of them target lycopene extraction. In comparison, β-carotene is targeted in nine studies (about 24%), whereas tocopherols by only two (5%). The interest in these compounds is mainly due to their biological and physiochemical properties, particularly their natural antioxidant activities.

Figure 2 shows the main components of interest present in tomato extracts. Below, we expand on the properties, applications and availability in different tomato sources, for the main families of compounds targeted by the SFE of tomato sources.

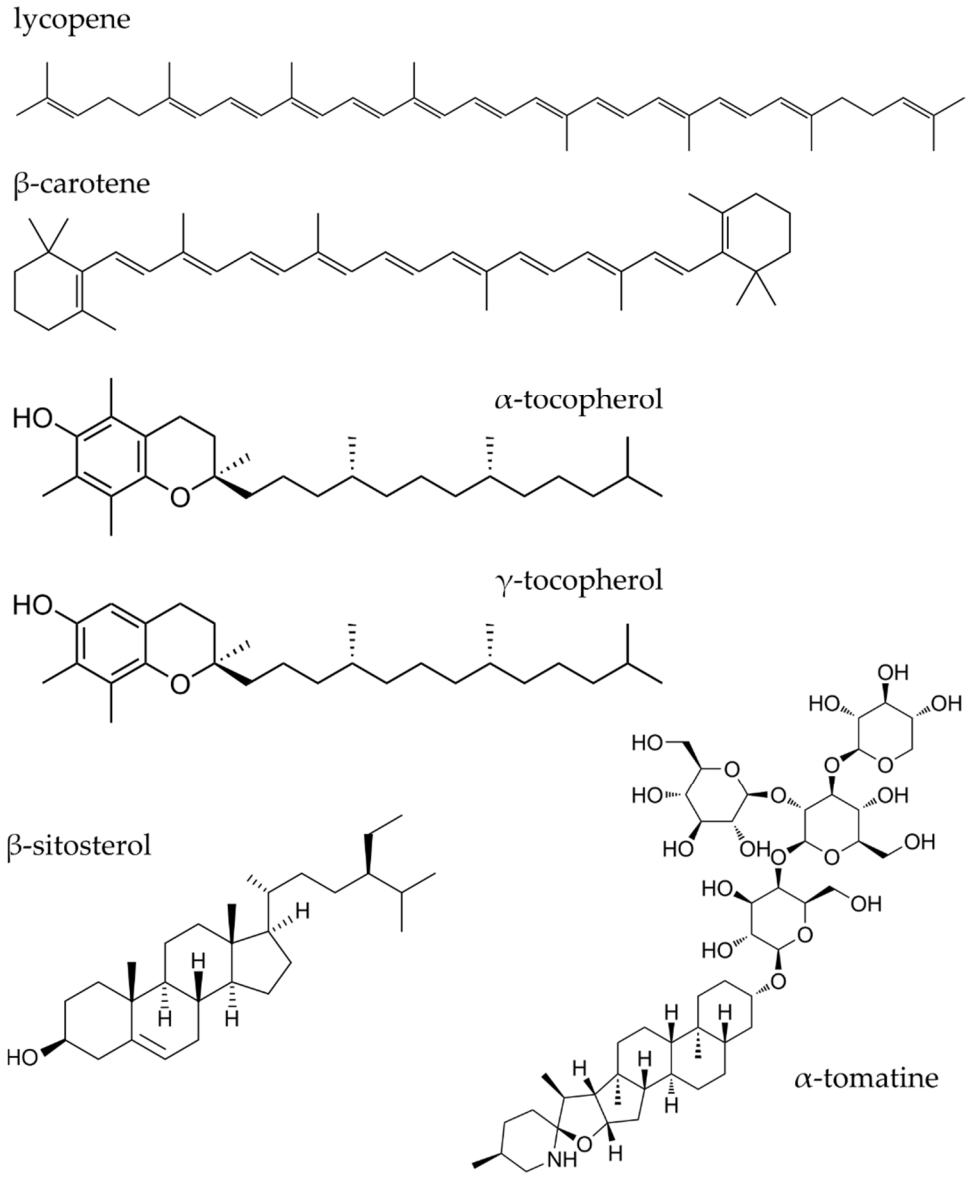


Figure 2. Structural formulae of relevant tomato extractables: lycopene, β-carotene, α-tocopherol, γ-tocopherol, β-sitosterol and α-tomatine.

3.1. Carotenoids (Lycopene and β-Carotene)

Lycopene and β-carotene are the most relevant carotenoids found in tomato. They have a molecular formula $C_{40}H_{56}$, are composed of eight isoprene units and contain a

high number of conjugated double bonds (eleven—see Figure 2). The lycopene molecule contains two more non-conjugated double bonds, whereas β-carotene has a six-membered ring at each end.

Lycopene is an important intermediate in the biosynthesis of many carotenoids and is responsible for the red pigments in plants. Although it is most abundant in tomatoes, it can also be found in other red fruits and vegetables, including carrots, guava, watermelons, grapefruits, apricots and papayas. In nature, lycopene exists predominantly in the *all-trans* form; however, it can suffer degradation by (*trans–cis*) isomerization and oxidation, due to its sensitivity to light, heat and oxygen [65]. It has been reported that the *cis*-lycopene isomers have a stronger in vitro antioxidant activity than the *all-trans* lycopene form [89]. Lycopene is the most abundant carotenoid in tomato, representing about 80% of all carotenoids in ripe tomatoes, with concentrations that can reach 50–100 mg kg^{-1} [26]. The content of lycopene in tomato depends on the species, growth and maturation conditions, and varies on the tomato part. For instance, ripe tomato skins can contain five times more lycopene than the pulp [26].

Several lycopene properties have been found which are beneficial to human health, namely, its high antioxidant activity and high singlet oxygen quenching ability. The antioxidant effects have been extensively demonstrated, both in vitro and in vivo [90,91]. Studies have also shown the role of lycopene in free radical inactivation and fat peroxidation inhibition [92], in minimizing the risk of cardiovascular diseases [93] and various forms of cancers [94], and in the pathophysiology of chronic diseases [95]. In addition to application as a nutraceutical, lycopene is also widely used as a food coloring.

β-carotene is responsible for the yellow or orange pigments in plants. It is found in gac fruit, mangoes, pumpkins and papayas. It is also present in tomatoes, although in lower amounts: about 3 μg/g of a wet sample [47]. β-carotene has been studied extensively due to its role in human nutrition as provitamin A as well as an antioxidant agent [66].

Other carotenoids are also found in tomato, namely, phytoene, phytofluene, ξ-carotene, γ-carotene and lutein. Similarly to lycopene and β-carotene, they are mostly found in tomato skins; however, their extraction is difficult to accomplish because they easily degrade in the presence of light, oxygen or heat [57].

Both lycopene and β-carotene are soluble in organic solvents; however, these are usually toxic and difficult to handle, leading to much interest in the development of cleaner processes for their extraction from natural sources, such as SFE. Gómez-Prieto et al. [57] studied the solubilities of several carotenes identified in tomato skin—namely, lycopene, β-carotene, phytoene, phytofluene and their geometric isomers—in supercritical CO_2 in the density range from 400 to 800 g L^{-1} and at three temperatures (40, 50 and 60 °C). For phytoene and phytofluene, solubilities increase with CO_2 density up to about 500 g L^{-1}, and then remain constant with a value of 75 g L^{-1}. In the case of β-carotene, a steeper increase in solubility is found, up to a CO_2 density of 700 g L^{-1}; then, solubility remains constant at a value of 300 g L^{-1}. Finally, lycopene presents a nearly exponential increase in solubility with CO_2 density, with values ranging from near zero to almost 1200 g L^{-1}. Differences in solubility were observed between the *trans* and *cis* isomers of lycopene [57]. At fixed densities, an increase in the temperature of extraction provoked an increase in the solubility of lycopene. The same behavior was found for the remaining carotenes; however, for these compounds, the final concentration plateau does not depend on temperature.

3.2. Tocopherols and Sitosterols

Tomato also contains significant amounts of tocopherols, mainly α-, γ-, and δ-tocopherols, and phytosterols, mainly β-sitosterol (see Figure 2).

Tocopherols are commonly referred to as saturated forms of vitamin E and are an essential part of the human diet. They are mostly recognized for their antioxidant activity and are used by the food and pharmaceutical industries. More recently, other relevant biological activities, such as anti-inflammatory properties, have been identified through mechanistic studies and clinical studies [96]. γ-tocopherol-enriched mixtures of tocopherols

have demonstrated a capability to inhibit the formation of colon, prostate, mammary and lung tumors in animal models, revealing potential applications in cancer prevention in humans [97].

The main sources of tocopherols are vegetable oils, seeds and nuts, such as almond oil, olive oil, sunflower oil, rapeseed oil, and soybean oil [98]. In tomato, α- and γ-tocopherols are the most common, mainly found in the seeds, which are a common residue after tomato processing [68]. Tocopherols are apolar molecules, and thus are easily soluble in nonpolar solvents such as *n*-hexane and supercritical carbon dioxide [68].

β-sitosterol is one of the known phytosterols, together with cholesterol, campesterol and stigmasterol. It has several reported nutritional and pharmacological activities, such as anxiolytic and sedative effects, anti-inflammatory, immunomodulatory, antibacterial, anticancer, hepatoprotective, lipid lowering effect, antioxidant and anti-diabetic effects, among others [99]. The main sources of β-sitosterol are lipid-rich or leguminous plants; for instance, nuts, avocados and olives [99]. In tomato pomace extract, β-sitosterol has been found in amounts ranging from 0.68 to 6.21 mg/100 g of dry material, with the higher contents obtained in SC-CO_2 extracts as opposed to organic solvent extracts [68]. β-sitosterol is hydrophobic and soluble in alcohols. It is thermally unstable and easily converted to oxidized products [99].

3.3. Other Compounds

Several other compounds of interest are present in tomato biomass, such as tomatine, tomatidine, chlorophyl *a* and chlorophyl *b*, although their amounts can vary widely through the tomato life cycle [100,101].

Tomatine is a glycoalkaloid mixture of α-tomatine and dehydrotomatine, in proportions of approximately 10:1, with reported health benefits in both animals and humans. These include the inhibition of cancer cells, anticarcinogenic effects in vivo, induced programmed cell death by reactive oxygen species (ROS) in the fungal pathogen, and a potential to protect against malaria [100]. Tomatine content varies significantly during the tomato maturation process. It is highest in green tomatoes and starts decreasing during the ripening process, being almost completely degraded when the fruit is ripe [101]. According to Kozukue et al., dehydrotomatine and α-tomatine content is highest ten days after flowering and drops by 16-fold in the subsequent ten days [102]. Despite its interesting bioactivities, there are no studies targeting the extraction of tomatine from tomato using supercritical fluids. This can be attributed to the fact that tomatine degrades quickly and most SFE studies utilize tomato sources late in the tomato life cycle, because they are usually byproducts of tomato processing in several industries.

4. SFE of Tomato

The compositions and yields of tomato extracts depend mainly on: (i) the type of tomato source material, which can be from different tomato parts (e.g., pulp, seeds and skins), from different maturation stages (e.g., ripe or green tomatoes), and from specific tomato cultivars (e.g., lycopene rich cultivars); (ii) the pretreatment applied before extraction, for instance, milling, freeze-drying and enzymatic digestion; and (iii) the SFE operating conditions, such as temperature, pressure, CO_2 flow rate, extraction time and the type and amount of cosolvent used. Below, we cover these aspects in greater detail.

4.1. Tomato Sources

The wide range of processed tomato products leads to different types of residues, such as peels, seeds, pulp and vascular tissues, and mixtures thereof. For instance, in the production of canned tomatoes, usually only the peel is removed, whereas for purees, pastes and juices, the seeds are separated as well. A combination of skins and seeds may be called paste waste [47] or, if it also contains vascular tissues, tomato pomace [75,80]. Seeds and skins are the predominant tomato morphological parts generated as residues, which can account up to 40% of the initial weight [3]. The tomato morphological parts

extracted with SFE were compiled and the results are presented in Figure 3. One may notice that peels and seeds are the most common tomato residues studied, specifically in 35% and 30% of the papers, respectively. Research focuses on the largest types of residues due to their larger availability, which potentiates the scale-up of the process, but is also due to the high content of carotenoids in skins and of seed oils containing phytosterols, proteins and fatty acids [103,104]. Notably, Figure 3 lists all the individual morphological parts mentioned, even when addressing combinations of several parts, such as pomace, which refers to the mixture peels and seeds, and can include pulp as well. In addition to peels and seeds, which account for 65% of the residues studied, these are followed by pomace with 13% and pulp, paste and puree with 11.7%. The remaining residues reported address tomato vascular tissues, the whole fruit and others. Even though the whole tomato does not represent a common residue, it has been studied by several authors, after distinct pretreatments.

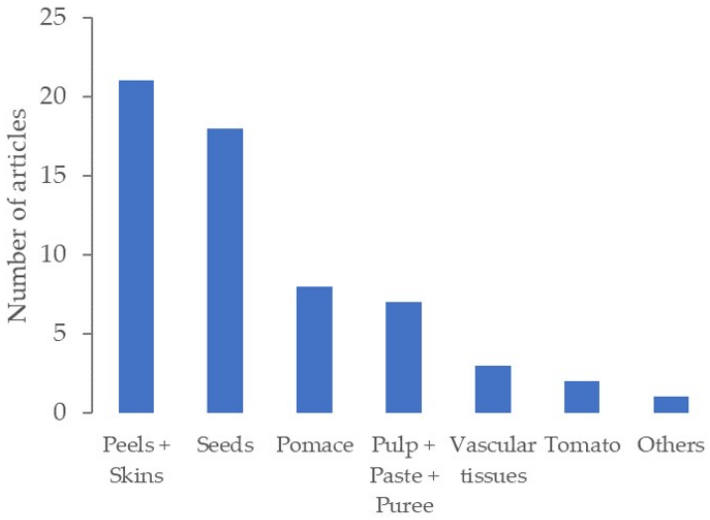


Figure 3. Distribution of research studies over the different morphological parts of tomato plant according to the data collected in Table 1.

As expected, depending on the tomato part, different oleoresin, lycopene, carotene yields are obtained by SFE. Vági et al. performed extractions using SC-CO_2 with different blends of peels and seeds, and obtained the highest oleoresin yield in seeds (246 g/kg at 500 bar/40 °C/240 min) and the lowest in peels. In terms of lycopene yield, Hatami et al. [83] demonstrated via experimental and mathematical modeling that it increased with the peel/seed ratio, 30/70 to 70/30, presenting a larger impact than temperature and pressure in the range of conditions studied (300–500 bar, and 40–80 °C).

Depending on the tomato cultivar, very different profiles of extractables can be found. A survey of lycopene content in several tomato cultivars found values ranging from 0.02 to 70 mg/100 g (wet basis) for gold sunrise yellow tomato and pear shape fresh tomato, respectively. Common red varieties (e.g., Cherry, Beefsteak and Tigerella) average around 3.3 mg/100 g (wet basis) [4].

As discussed in Section 3, the amount of desired extractables in the source material varies greatly during the tomato maturation process. Ripe tomato contains higher levels of lycopene and carotene, but little to no chlorophyl and tomatine. On the other hand, unripe tomatoes contain tomatine and chlorophyll, but no lycopene and β-carotene [101].

4.2. Pretreatments

Tomato waste treatments before extraction also differ with the type of waste. For instance, when the starting material is whole tomatoes, sample preparation begins with tomato washing to remove any dirt or impurities, followed by crushing and peeling, which can occur in reverse order. After these steps, the separation of the solids (skins, seeds,

vascular tissues) from the pulp and juices is performed by pressing, filtration and/or sieving. At this stage, the most common residues produced in the food industry can be obtained. Individual morphological parts can be isolated and studied individually as well as in combination with others. Nonetheless, before the extraction with supercritical fluids, some additional steps can be employed to enhance the extraction performance.

Plant material has a large content of water, and tomatoes especially. The moisture content in the processing residues can surpass 80 wt.% [70], and sun-dried tomatoes can contain 50–60 wt.% of water [50]. However, it is known that high contents of water do not enhance the performance of SFE using CO_2. In fact, Vaspollo et al. [50] and Nobre et al. [70] reported only trace amounts of lycopene in extracts produced from tomato materials with high moisture contents. The high contents of water explain the low solubility of carotenoids, but they also change CO_2 properties, such as the surface tension, which can hinder its penetration ability. Furthermore, the presence of water can generate a thin film between the matrix and the supercritical fluid, whereas its removal can improve the access of solutes through the pores of the matrix. It can be argued that high water contents swell the matrix, which can favor the extraction but, at the same time, this can increase the path solutes need to travel [26]. Reducing the content of water to values close to 10 wt.% seems to favor the extraction performance [26]. Nonetheless, extensive drying can also lead to the degradation of tomato solutes as well as cause the collapse of the vegetable cells, blocking its solutes, thus resulting in lower recoveries, as reported by Nobre et al. [70] for the lowest water content studied, 4.6 wt.%.

The drying of tomato samples has been reported using ovens, air-drying, sun-drying, freeze-drying and the addition of silica gel. Once the moisture content reaches the desired level, the most common next step is particle size reduction. The milling of the biomass, whether it is seeds, tissues or skins, eases the release of solutes from the cells. For large, intact particles, the solutes need to diffuse from the inside to the surface of the particle to reach the solvent, which is a slow process. This limitation to mass transfer motivates particle size reduction methods so that a larger fraction of cells is broken, easing solute release and increasing the contact area between the particles and the solvent, thus enhancing the rate of extraction. Roy et al. [60] demonstrated the effect of particle size reduction for tomato seeds, achieving a total yield more than three times higher when reducing the particle size from 1.02 to 0.25 mm. Baysal et al. found similar results regarding the yields of lycopene and β-carotene, which increased by five and four times, respectively, when the tomato paste waste was milled to a diameter of 3 mm. In the work of Kehili et al. [79], the SFE of intact and ground tomato peels was tested (see Figure 4). It was observed that, for a particle reduction from 1 mm to 300 µm, the oleoresin yield obtained at 400 bar and 50 °C, after 105 min of extraction, increased from 3.97% to 4.86%, respectively. Furthermore, after 10 min of extraction, whereas the intact particles oleoresin yield reached 36% of its total recovery, the ground particles had already reached 82% of the respective total value, which evidences the impact of particle size reduction on the extraction rate. Nobre et al. [70] observed that, when using supercritical CO_2, the reduction in particle size of a mixture of tomato seeds and peels from 0.72 mm to 0.36 mm did not affect the recovery of lycopene. However, when the size was further reduced to 0.15 mm, the lycopene recovery increased by 78%. In a later work on mixtures of tomato skins and seeds, Nobre et al. [46] noticed that, although the decrease in particle size from 0.56 mm to 0.15 mm did not improve the final recovery of lycopene, it did so in the initial stages of the extraction, with the smaller particles attaining roughly double the lycopene recovery of the larger ones. Furthermore, whereas the recovery obtained for the 0.15 mm particles achieved its maximum at the first measurement, a mass of solvent roughly six times higher was necessary for the 0.56 mm particles to reach an identical recovery. These results suggest that small particle sizes are desirable to reduce the intraparticle mass transfer resistance. However, for particles too small, uneven extractions can occur due to channeling effects of the fixed biomass bed. Sabio et al. [66] reported channeling to be the probable cause of the decrease in lipids, lycopene and carotene extraction yields from mixtures of tomato

seeds and skins. Additionally, particle size reduction requires that specialized equipment is added to the process. In certain cases, this may not be economically advantageous in comparison with the extraction of biomass as it is. SFE of tomato pomace with no milling (the only pretreatment was drying) using pure CO_2 at 300 bar/60 °C provided a total yield of 30.6 g/kg of biomass (see the Supplementary Materials). This is significantly lower than the yield of ca. 250 g/kg reported in the literature [80,82].

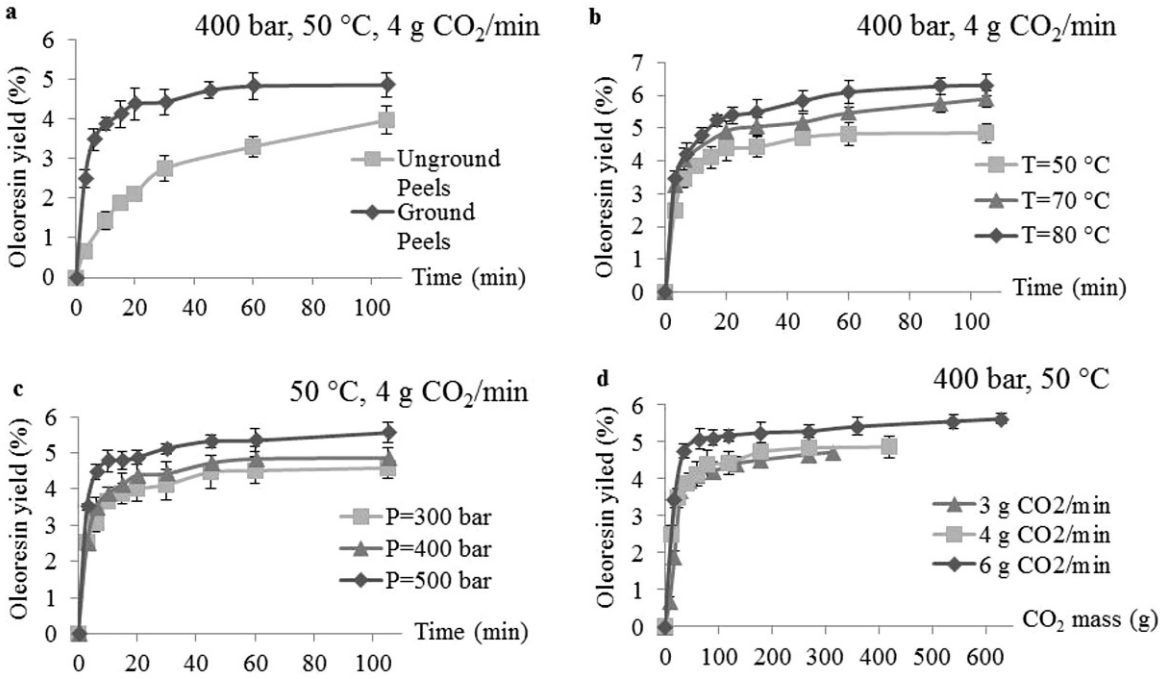


Figure 4. SFE curves (yield vs. time) of tomato peels (10 g) with SC-CO_2 to illustrate the effect of (**a**) particle size, (**b**) temperature, (**c**) pressure, and (**d**) flow rate. Reproduced from [79].

Less common sample treatments include the use of enzymatic digestion. Enzymes will degrade cell walls and facilitate both solvent penetration and solutes release. Lenucci et al. [78] reported a threefold increase in lycopene concentration in SFE extracts (500 bar/86 °C/4 mL min^{-1}) and similar total extraction yields after tomato pretreatment with plant cell wall glycosidases. The enzyme digestion also increased the attainable extractor loading significantly but, as it was reported, even without the enzyme treatment, fluid channeling was observed. This was countered by the addition of an oleaginous co-matrix (grounded hazelnut seeds) that decreased the packing density of the matrix. Nevertheless, the viability of this treatment is highly dependent on the enzyme cost.

4.3. Supercritical Fluid Extraction Conditions

4.3.1. Pressure

Pressure is one of the most important parameters in SFE, because it can drastically change the supercritical fluid properties. This can be observed in Figure 5, where the experimental conditions of pressure and temperature from the studies listed in Table 1 are presented along with constant CO_2 density lines (obtained with PC-SAFT equation of state). About 82% of the pressures listed lie between 100 and 400 bar, which seems to be a typical pressure range for the SFE of vegetable matrices [37]. Even in this narrow pressure range, CO_2 properties, such as density, can change significantly. For instance, at 60 °C, the density of CO_2 can be 305 and 880 kg m^{-3}, at 100 and 400 bar, respectively.

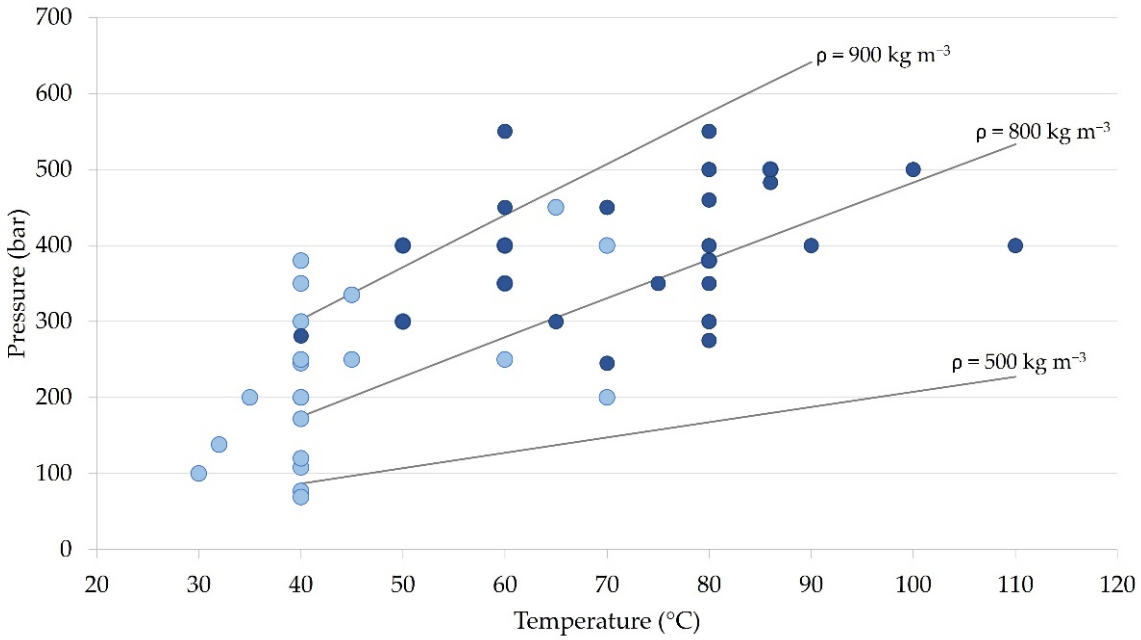


Figure 5. Operating conditions (pressure and temperature) of the studies listed in Table 1 using SC-CO_2. Light blue and dark blue dots represent the regions of lower and higher CO_2 densities in each work, respectively. Lines of CO_2 constant density (calculated with PC-SAFT equation of state) are indicated in gray.

This increase in density imparts an increase in the solvating power of the fluid, which can favor the solubility of the solutes, as in the case of β-carotene [105]. Roy et al. [61] observed a strong increase in the SFE total yield of oil from tomato seeds and in the extraction rate when pressure increased from 108 to 245 bar. Furthermore, the extracts obtained at the highest pressures exhibited higher wax and yellow pigment contents, which was attributed to the changes in solute solubility in SC-CO_2. The effect of higher pressures on the oleoresin yield was tested by Kehili et al. [79] in the pressure range from 300 to 500 bar at 50 °C (see Figure 4c). From 300 to 400 bar, the oleoresin yield increased from 4.58 to 4.86%, respectively, whereas at 500 bar, the oleoresin yield reached 5.56%. Nobre et al. [46,70] studied the effect of pressure on the recovery of lycopene from tomato seeds and skins using supercritical CO_2 or ethane. For SC-CO_2, the decrease from 300 to 200 bar lowered the lycopene recovery from 93% to 30% and significantly slowed down the extraction rate. The same effects were observed with supercritical ethane. These results were explained by the lower lycopene solubility and solvent density at lower pressures, and by the potential competition between carotenoids and lipids from the seed oil, because these have a higher solubility and are first extracted. Rozzi et al. [64] studied the effect of pressure on the recovery of lycopene, tocopherols and lipids from tomato seeds and skins. For lycopene and α-tocopherol, higher pressures favor its recovery, whereas for δ-tocopherol and lipids, pressure did not significantly influence the results. For the valorization of tomato juice byproducts, Egydio et al. [72] observed a positive, but not statistically significant, effect of pressure on the lycopene recovery, and the maximum antioxidant activity was also obtained at the maximum pressure tested: 350 bar. Gomez-Prieto et al. [65] explored the effect of density on the extraction of carotenoids from tomato skin and pulp without seeds, and reported that the effect of low to intermediate pressures (77–281 bar) overshadows the effect of temperature increase on the yield, due to the balance between higher solute vapor pressures and lower CO_2 density. Increasing the pressure at 40 °C, i.e., with higher CO_2 densities, more carotenoids were obtained, namely, phytoene, phytofluene, β-carotene and lycopene, as well as higher total recoveries. Furthermore, it was stated that the different yields obtained for the lycopene isomers may be a result of solubility rather than isomerization reactions occurring in the presence of SC-CO_2. A

statistical analysis by Vagi et al. showed that pressure is the most significant variable for the extraction yield of tocopherols from tomato pomace. Lower pressures were favorable to the tocopherol yield, with the best results obtained at 300 bar (bottom end of pressure range) and 80 °C.

It is known that pressure favors the solvent density and its solvating power, which can increase solute solubility and the rate of extraction. Furthermore, by operating at higher pressures, a lower amount of CO_2 may also be necessary for the same extraction yields [105]. On the other hand, as extraction pressure increases, solvent diffusivity decreases. Moreover, excessive pressures can reduce the pore size of a sample and increase its packing, hindering the extraction performance [106]. Additionally, it is useful to know the conditions for maximum solubility of the target solutes, for instance, the maximum solubility of β-carotene in supercritical CO_2 is achieved at approximately 500 bar [107].

4.3.2. Temperature

Temperature is also a critical parameter for the supercritical solvent properties, and thus, SFE. Most of the studies (88%) compiled in Table 1 were performed within 40–80 °C, as can be observed in Figure 5. Once again, this is a common temperature range for the SFE of vegetable matrices [37]. Similarly to pressure, temperature strongly affects the density of supercritical CO_2, especially at lower pressures. For instance, an increase from 40 to 80 °C reduces the CO_2 density from 640 to 230 kg m^{-3} at 100 bar, whereas at a pressure of 400 bar, the density varies from 945 to 812 kg m^{-3}. Nonetheless, temperature also affects the vapor pressure of the solutes, which typically increases exponentially with temperature. These two effects can either balance each other or not, which emphasizes the importance of experimental optimization.

Cadoni et al. [62] extracted tomato skins and seeds at 275.8 bar and reported that, at low temperatures (40 °C), the SC-CO_2 is very selective towards β-carotene, with only small amounts lycopene extracted. When temperature increased from 40 °C to 80 °C, a 17-fold lycopene yield increase was verified, whereas the β-carotene yield doubled. These values represent 83.6% and 92.4% recoveries of the reference yields for the hexane:acetone Soxhlet extraction of lycopene and β-carotene, respectively. These results are explained by the increase in the compounds' solubility at higher temperatures. Kehili et al. [79] assessed the effect of temperature on the oleoresin yield from tomato peels (see Figure 4b). At 400 bar, the temperature increase from 50 to 80 °C boosted the oleoresin yield from 4.86% to 6.31%. Even though the temperature increase lowered the CO_2 density by 11%, the increase in solute vapor pressure was the dominant effect. Nonetheless, the extraction curves obtained were similar and only started to separate after the initial period of extraction, which, at 20 min, already accounted for up to 80% of the oleoresin yield. The major differences were observed during the diffusion-controlled period. The influence of temperature on the lycopene and β-carotene recoveries was also favorable, increasing from 40.27% to 60.85% and 44.27% to 58.8%, respectively. Urbonaviciene and Viskelis [80] optimized the oleoresin and lycopene extraction yields from mixtures of peels, vascular tissues, seeds and small amounts of pulp. For both responses, temperature (40–80 °C) was the second most significant factor, following pressure. Temperature showed a positive effect on the oleoresin extraction yield, whereas it had a negative effect on the lycopene extraction, which was attributed to thermal degradation. For temperatures higher than 80 °C, SFE of tomato skins was performed by Ollanketo et al. [63], who obtained significantly better lycopene recoveries at 400 bar and 110 °C. These authors also state that no change on the lycopene isomer composition was observed at the tested temperatures, in the range from 60 to 110 °C.

As discussed above, the increase in temperature can be advantageous for the recovery of carotenoids as well as the total extraction yield. Due to the effects on the supercritical solvent and solute solubility, its optimization for the extraction process productivity and selectivity purposes, as well as avoiding target compounds thermal degradation, is a crucial step.

4.3.3. Supercritical Solvent Modifier (Cosolvent)

The choice of pressure and temperature of extraction is a critical step for SFE because it allows the tuning of CO_2 properties to target the desired families of compounds. However, the SFE efficiency can be further improved with the addition of low contents of a modifier (also called a cosolvent or entrainer), such as organic solvents, vegetable oils and water. The choice of the modifier aims to enhance the solute solubility in the supercritical solvent by modifying its polarity, and improvements in the solvent properties favor the extraction performance. The matrix being extracted is also affected and can swell with the addition of modifiers, easing the solvent penetration and the solute extraction. Among the different organic solvents tested as CO_2 modifiers, the most common for the extraction of natural products is ethanol [37]. From Table 1, amongst the studies employing modifiers, over half included ethanol. As shown by Brunner and Peter [108], the solubility of solutes with low volatility is increased by the addition of ethanol as a CO_2 entrainer.

Cadoni et al. [62] tested the effect of four entrainers (chloroform, *n*-hexane, ethyl ether and ethanol) to improve the lycopene and β-carotene recoveries from ground tomatoes, skins and seeds. Chloroform and *n*-hexane gave the best results, but chloroform traces were found in the extracts, which is a key drawback of using toxic organic solvents as modifiers. Watanabe et al. [52] used 5 wt.% of ethanol, hexane and ethyl acetate as CO_2 entrainers for the SFE of lycopene from tomato pulp. Ethanol and ethyl acetate solvents are considered "greener" for food and pharmaceutical applications, in comparison with conventional solvents, such as hexane, dichloromethane or chloroform [109]. Lycopene recoveries ranged from 5.2 to 8.7 wt.% for ethanol and ethyl acetate, respectively, showing a great increase from pure CO_2, which obtained a recovery of 1.6 wt.%. Baysal et al. [47] modified CO_2 with ethanol (5, 10 and 15 wt.%) and compared the results with pure CO_2 for the recovery of lycopene and β-carotene from tomato paste waste. With 5 wt.% of ethanol as an entrainer, the lycopene and β-carotene recovery increased approximately 145% and 16%, respectively, in comparison to pure SC-CO_2. The further increase in ethanol content resulted in lower recoveries of both compounds and, at 15 wt.%, the results were lower than those for pure CO_2. The solubility of β-carotene in pure and modified CO_2 was studied by Sovova et al. [110], who observed that the addition of 0.3 to 2.4 wt.% of ethanol or vegetable oil to CO_2 significantly increased β-carotene solubility. However, the increment obtained by the ethanol was four times higher than that with vegetable oil. Kassama et al. [48] optimized the SFE of lycopene from tomato skin using 5 to 15 wt.% ethanol as an entrainer. Although ethanol content did not show a significant effect for the lycopene yield, a synergetic effect between ethanol content and temperature was observed. Furthermore, the effect of ethanol content on the recovery of lycopene was indirectly proportional to temperature, which was explained by the degradation of lycopene at higher temperature, although the ethanol contents employed did not increase the critical temperature of the mixture further than the lowest temperature selected [111]. Even though many organic solvents can be tested to change CO_2 properties, ethanol remains one of the most important, because it can be easily removed and is acceptable for food and pharmaceutical applications. Nonetheless, its content must be always optimized so that the maximum extraction performance is obtained and balanced with the economic costs implied.

The use of natural modifiers avoids the concerns about extract contamination with toxic organic solvents while enhancing the SFE process performance. Such is the case of vegetable oils, which do not need to be recovered at the end of the extraction process. Vegetable oils from different sources were mostly tested for the recovery of lycopene from tomato skins and seeds. For instance, hazelnut oil significantly improved the recovery of lycopene and enhanced its stability (i.e., avoided its degradation) [50]. Barros et al. [51] added avocado pulp to tomato pomace and observed an increase in the extraction yield of lycopene, as a result of the avocado oil extracted. However, lycopene concentrations were lower, because it is diluted in the extract. Watanabe et al. [52] tested eight edible vegetable oils as entrainers, namely, linseed, soybean, corn, sesame, rapeseed, hazelnut, sunflower seed and olive oils. Hazelnut oil led to the highest lycopene recovery (21.6 wt.%),

showing a significant improvement in relation to pure CO_2 (1.6 wt.%) as well as CO_2 modified with ethanol, hexane and ethyl acetate, which did not achieve more than 8.7 wt.% recoveries. The authors also tested the addition of water, but it only slightly improved the lycopene yield, reaching 2.3 wt.% [52]. It is known that the addition of water can help the swelling of the matrix and thus ease the recovery of solutes, even though it is reported that for biomass moisture contents higher than 18%, clogging problems can occur [112]. In a similar study, Shi et al. [49] tested the modification of CO_2 with vegetable oil (canola oil), an organic solvent (ethanol), water and their combinations. When tested individually, the three modifiers' contents ranged from 5% to 15%, with 10% of olive oil producing the best recovery. The effect of combinations of modifiers was assessed with multiple mixtures of two and all three, with contents ranging from 5 to 10 wt.%, given a maximum content of all modifiers of 15%. Olive oil and ethanol showed the best results, reaching a lycopene recovery of 73.3%, using 10 wt.% of both. Even though the addition of water can increase CO_2 polarity and swell the matrix pores, it is important to note that water is already present in most biomass (as moisture content). It is worth noting that most studies did not calculate/check the solubility of each cosolvent in the supercritical CO_2, and report cosolvent contents above the maximum value permitted by the equilibrium. This is usually the case with water.

The group of solvents typically used as modifiers in SFE is small, with ethanol being the most common. This is typical in all SFE and not specific to tomato. We have performed the SFE of tomato (300 bar/60 °C/12 g/min CO_2/6 h/no particle size reduction) using 10% ethyl acetate as a cosolvent and compared the results with pure CO_2 and with 10% ethanol (see the Supplementary Materials). From Figure 6, which shows the extraction curves for these three cases, we can see that ethanol provides the highest total yield (3.82%) compared with 3.52% and 3.06% for ethyl acetate and pure CO_2, respectively. However, it appears that ethyl acetate produces a faster extraction rate in the first 2 h. This can be a significant improvement in an industrial process where the extraction is optimized for productivity; thus, only the higher extraction rate phase is used. Similar results have been found for other biomasses such as *Vitis vinifera* leaves [33].

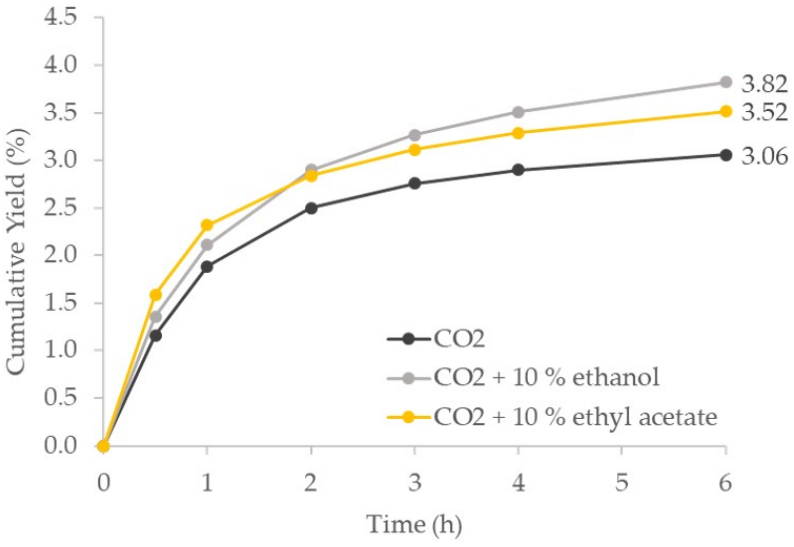


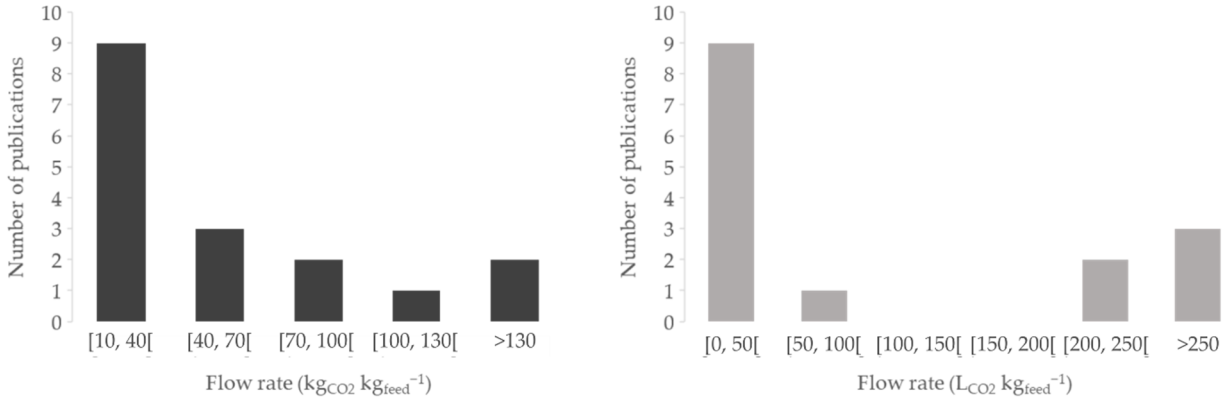
Figure 6. Extraction curves of tomato pomace using pure CO_2, CO_2 with 10% ethanol and CO_2 with 10% ethyl acetate at 300 bar/60 °C/12 g/min CO_2/6 h with no particle size reduction.

4.3.4. Flow Rate and Extraction Time

The supercritical solvent flow rate indicates the amount of solvent passing through the extractor for a given time and may be essential for the improvement of extraction efficiency. It is commonly controlled by a liquid pump or compressor, together with a restrictor or a back-pressure regulator (BPR) installed after the extractor. In the case of low flow rates,

the velocity of the solvent is lower, resulting in higher residence times and higher external resistances to mass transfer, as the thickness of the diffusion film around the particles increases. Solvents can reach saturation faster along the bed and the solubility of the extract can limit the extraction rate, reducing the process yields. With increasing flow rates, the external resistances to mass transfer decrease and internal diffusion prevails, which ensures higher yields of extraction. However, excessive solvent flow rates offer no gain to the whole process after the external film diffusion is eliminated and the solute concentrations in the bulk become negligible. At this moment, increasing flow rate only increases solvent and operating costs.

The flow rates used in the studies presented in Table 1 are compiled in Figure 7. The mass and volume flow rates were normalized by the amount of sample used in each study so that the effect of scale was eliminated. One may observe that the most common values for solvent flow rates are within 10 to 40 $kg_{CO_2}\,kg_{feed}^{-1}$ and 0 to 50 $L_{CO_2}\,kg_{feed}^{-1}$. These values are close to those previous validated in scale-up studies for the SFE of vegetable biomasses [113].



(**a**) (**b**)

Figure 7. Typical mass (**a**) and volumetric (**b**) flow rates used in research on tomato SFE.

Rozzi et al. [64] tested the effect of solvent flow rate on the SFE of lycopene from tomato seeds and skins. At 344.7 bar and 86 °C, CO_2 flow rates ranging from 2.5 to 15 mL min^{-1} decreased the lycopene yield from 4.59 to less than 1.0 μg $g_{raw\ material}^{-1}$. The lower yield may be explained by the channeling and uneven distribution of the CO_2 at the highest flow rates.

Malik et al. [77] studied the effect of CO_2 flow rates (4, 8 and 12 mL min^{-1}) on the extraction of carotenoids from tomato pomace, at 278 bar and 80 °C. Increasing the flow rate from 4 to 8 mL/min increased the lycopene recovery from 76.60% to 82.50% but for 12 mL/min, the lycopene recovery dropped to 79.0%. In case this drop is statistically significant, it may be attributed to the high solvent velocity that may, once again, cause channeling. Kehili et al. [79] also tested the SFE of carotenoids from tomato peels (400 bar, 50 °C) using three solvent flow rates (3, 4 and 6 g/min) and reported an increase in total extraction yield from 4.72% to 5.62% (see Figure 4d). The extraction curves obtained reveal two distinct periods, starting with a constant extraction rate branch for the different flow rates, resulting from the extraction of external and more available solutes. The second period is a falling extraction rate phase, characterized by the extraction of more internal solutes, which need to diffuse to the external surface of the particle and then to the bulk. The same extraction periods were observed by Pellicano et al. [84], Bruno et al. [81], and Urbonaviciene and Viskelis [80]. On a different note, Nobre et al. [46] did not observe significant differences when testing various solvent superficial velocities for the supercritical ethane extraction of lycopene from tomato waste residues. The same was concluded by Machmudah et al. [3], who found that different solvent flow rates did not affect the lycopene, β-carotene or oil recovery from seeds.

The duration of SFE assays is another important parameter to study. It is known that the longer the extraction time, the higher the extraction yield; however, as illustrated in Figure 8, the extraction rates differ over time. In the first period, the available solutes are extracted at a maximum and constant extraction rate. Then, the process fades into a diffusion-controlled phase, with lower extraction rates, where the solutes have to diffuse from the inside to the outside of the particles and are then transferred to the bulk. Commonly, the optimum extraction time is at the intersection point of the asymptote of the constant extraction rate period and the plateau achieved in the diffusion-controlled phase. Even though the highest yield will not be achieved, the maximum productivity should be.

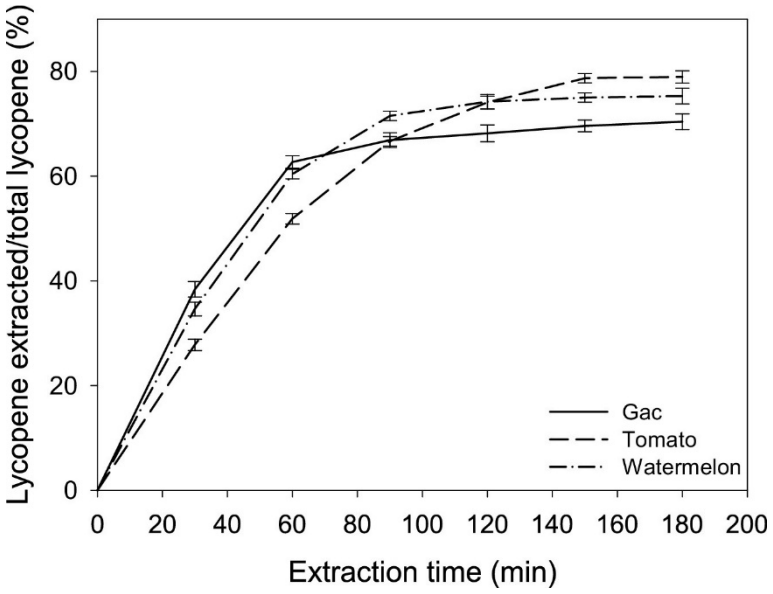


Figure 8. Supercritical CO_2 extraction yield over time for three fruits (gac, tomato and watermelon). Reproduced from [81].

Nobre et al. [70] studied the SFE of *trans*-lycopene from mixtures of skins and seeds from tomato residues using different CO_2 flow rates, 0.26, 0.59 and 1.05 g/min, at 300 bar and 60 °C. The results were compared in terms of *trans*-lycopene recovery by the time of extraction and amount of solvent. It was concluded that the lower flow rates were similar and more favorable for *trans*-lycopene recovery. In contrast, the highest flow rate attained lower recoveries for the same amount of CO_2 spent, which the authors attributed to channeling effects and not reaching equilibrium.

5. Final Remarks

Tomato residues are a readily available vegetable matrix with substantial exploitation potential for the food, nutraceutical and pharmaceutical sectors. Given their high concentrations in the source material, carotenoids (namely, lycopene and β-carotene) are clearly identified as the most interesting target for supercritical fluid extraction. Although their chemistry has long been known, the role of lycopene and β-carotene in human health is only now being studied with actual clinical and dietary intervention studies. In this context, SFE presents some relevant advantages over other extraction methods, because it can provide an environmentally safe process where the mild CO_2 critical conditions are suitable for working with thermolabile compounds, as is the case of carotenoids. Furthermore, the extraction can be tuned to selectively target certain components by modifying the pressure and temperature and by adding a cosolvent. The design of optimized processes for tomato extraction are well reported in the literature, mainly through a combination of modelling and the application of design of experiments methodologies. These studies have identified the effects of the main operating conditions on the yield and recovery of total oils or target

compounds and provided optimum operating conditions that are a good starting point to expedite the scaling up of industrial processes.

Supplementary Materials: The following are available online at https://www.mdpi.com/article/10.3390/pr10010028/s1, Figure S1: Extraction curves of tomato residues using pure CO_2, CO_2 with 10% ethanol (EtOH), and CO_2 with 10% ethyl acetate (EtAc), Table S1: SFE experimental conditions and total yields obtained. Fixed conditions: 300 bar/60 °C/12 g min^{-1}/6 h.

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