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Enhancing Lycopene Extraction and Isomer Selectivity From Tomato Pomace: A Study of Particle Size, Drying Technique, and Supercritical Fluid Extraction Processing Variables

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ABSTRACT

The growing demand for functional ingredients and the food industry waste burden have increased interest in recovering valuable compounds, such as lycopene, particularly its bioavailable form (*cis*), from tomato pomace, a by-product of the tomato industry. Supercritical fluid extraction (SFE) using supercritical CO_2 offers an eco-friendly alternative to conventional solvent extraction (SE) methods. This study evaluated the effects of drying method (freeze-drying [FD] vs. oven-drying [OD]), particle size (<0.5 vs. <2 mm), thermal pretreatment (1 h at 120°C), and extraction temperature (50°C vs. 90°C) on lycopene extraction using SFE at 200 bar. A conventional SE with hexane–acetone–ethanol (2:1:1 v/v) was used as a reference. Lycopene yield and *cis*-isomer content obtained by SE and SFE were quantified using high-performance liquid chromatography. Extraction temperature was the most influential factor: SFE at 50°C yielded significantly more lycopene than at 90°C. At 50°C, lycopene yield increased by approximately 1.6 times with both particle size reduction and thermal pretreatment. FD also enhanced yield, showing a 1.2–1.3-fold increase compared to OD. Although overall lycopene yields were lower with SFE compared to SE, the proportion of *cis*-isomers was consistently higher in SFE extracts across all treatments. In conclusion, the optimal SFE conditions for lycopene extraction from tomato pomace, balancing high yield and enhanced *cis*-isomer content, include low extraction temperature (50°C), reduced particle size, thermal pretreatment, and FD.

1 | Introduction

Tomatoes (*Lycopersicon esculentum*) are among the most widely consumed vegetables globally, with their processing generating an estimated 8 million tons of waste each year. A major by-product of tomato processing is tomato pomace, the material remaining after crushing and sieving, which includes peels, seeds, and occasionally pulp (Lu et al. 2019). Tomato pomace, accounting for approximately 1.5%–10% of fresh tomato weight, is rich in bioactive compounds, especially lycopene, making it a promising candidate for valorization and upcycling (Silva et al. 2019; Trombino et al. 2021). Lycopene accumulates in the tomato skin during the ripening process, giving tomatoes their characteristic red color (Zuorro et al. 2011). This compound possesses strong antioxidant activity, which is nearly twice that of β-carotene and 10 times greater than tocopherol (Caseiro et al.

2020; Grabowska et al. 2019). The high antioxidant activity of lycopene is associated with a reduction in oxidative stress, and some studies suggest that it may have a preventive effect against cardiovascular and carcinogenic diseases (Przybylska 2020).

The conventional method for extracting lycopene from tomatoes is organic solvent extraction (SE) using, for example, hexane, chloroform, and acetone (Poojary and Passamonti 2015). This conventional method requires long extraction times and uses large amounts of toxic organic solvents, necessitating extensive and expensive multistep treatments to completely remove the solvent from the final product (Reverchon et al. 2022).

Supercritical fluid extraction (SFE) offers a more environmentally friendly alternative to conventional SE, producing extracts free from toxic residues (Sabio et al. 2003). SFE typically uses supercritical CO_2 (SC–CO_2) as a solvent, which is nontoxic, available at low cost, and highly pure (Sabio et al. 2003). In addition, this process reduces the required extraction time and concentration of organic compounds in the resulting extracted compounds (Topal et al. 2006). SFE is based on extraction at critical pressure and temperature of CO_2 to enhance the solvating power of the solvent, and its properties can be changed over a wide range by pressure and temperature, allowing a selective extraction (Papaioannou et al. 2016). During the extraction process, SC–CO_2 is dense and behaves like a liquid, allowing it to penetrate different matrices and solubilize lycopene. SFE has been widely studied for lycopene extraction from various tomato matrices, including juice (Egydio et al. 2010), pulp (Watanabe et al. 2018), pomace (Scaglia et al. 2020), and peels (Mihalcea et al. 2021; Pellicanò et al. 2020). Optimizing the extraction process by modifying the extraction temperature, a factor that influences solubility in CO_2, is crucial to enhancing lycopene yield.

In carotenoid extraction processing, it is essential to consider, together with the yield, also the isomerization, which can be greatly influenced by the physical conditions. Lycopene has 13 double bonds (11 of which are conjugated), and it is predominantly found in its all-*trans* form (80%–97% in tomato) (Honest et al. 2011). Isomerization of these double bonds from *trans* to mono- or poly-*cis*-isomers can occur due to various factors, including light, thermal energy, and food processing involving heat, oil, or dehydration. This isomerization results in a mixture of *cis*-isomers, such as 5-*cis*, 9-*cis*, 13-*cis*, and 15-*cis*, which is generally desirable because *cis*-isomers have a stronger antioxidant effect and, more importantly, a higher bioavailability than the *trans* isomer (Colle et al. 2010; Honest et al. 2011). Numerous studies have investigated the effects of adding oil as CO_2 cosolvent (Shi et al. 2009; Watanabe et al. 2018), grinding (Reverchon and De Marco 2006), and adjusting SFE process conditions like pressure and temperature (Egydio et al. 2010; Shi et al. 2009; Vallecilla-Yepez and Ciftci 2018) on lycopene yield and isomerization pattern. However, the effect of these processes, both before and during SFE, on the yield and quality of lycopene extracted from tomato peels has not been studied in detail (Machmudah et al. 2012), especially when considering the combined influence of different variables. The aim of this research was to investigate the multifactorial effects of tomato pomace particle size and drying method in combination with SFE processing parameters like thermal pretreatment and extraction temperature on the yield and isomeric form of lycopene.

2 | Materials and Methods

2.1 | Materials

The raw materials (tomato pomace), consisting of tomato peels, seeds, and stems, were kindly provided by the company LaFiammante (Buccino, Salerno, Italy). Olive oil (mild) (Jumbo Supermarkten B.V., Veghel, the Netherlands) was purchased from the grocery store. Lycopene analytical standard (purity high-performance liquid chromatography (HPLC) ≥95%) was bought from Extrasynthese (Genay, France). The solvents used for HPLC analysis and SE were all of analytical grade.

2.2 | Methods

2.2.1 | Sample Preparation

2.2.1.1 | Drying. Frozen tomato waste pomace retained in the refinery step of tomato puree production was dried using two different methodologies: freeze-drying (FD) and oven-drying (OD). For FD, the frozen tomato pomace was first thawed to room temperature and mixed with olive oil to achieve a mixture of 1 g oil per 100 g of raw wet material, as reported by Shi et al. (2009). The tomato waste, including the oil, was then freeze-dried using a freeze-dryer (Edwards Lyofast S08, Liozzano dell'Emilia, Italy).

For OD, the frozen tomato pomace was thawed in a refrigerator at 7°C for approximately 24 h before drying. The thawed sample was divided into portions of approximately 200 g and placed into aluminum trays. It was dried in an incubator at 60°C with 40% ventilation for 44 h until the moisture content was reduced to less than 10%. After drying, olive oil was added by manually mixing it in a bowl with a kitchen spatula. The amount of oil added was proportional to the raw material used before drying, maintaining the same oil-to-raw-matter ratio (1% w/w oil per raw material) as in the freeze-dried samples. The oil was added during the pretreatment as a cosolvent to help the extraction through SFE, as reported by Shi et al. (2009).

2.2.1.2 | Grinding. OD and freeze-dried tomato pomace were ground using a rotor mill (PULVERISETTE 14, Fritsch, Idar-Oberstein, Germany). This mill allows for producing different particle sizes by adjusting the grinding speed and using various mill rings. In this specific case, by adjusting the grinding speed and employing two sieve rings (0.5 and 2 mm), powders with two distinct particle sizes were produced: <0.5 and <2 mm.

2.2.1.3 | Thermal Pretreatment. For the isomerization step via a thermal pretreatment, ±60 g of ground, dried material was dispersed in aluminum trays. The trays were covered with cardboard lids to limit moisture evaporation. They were then put in an incubator at 120°C for 1 h.

2.2.2 | Processed Tomato Pomace Characteristics: Moisture and Fat Content

2.2.2.1 | Moisture Content. The water content of the samples was determined using the Moisture Analyzer MA37 (Sartorius Lab Instruments GmbH & Co. KG, Germany) in triplicate.

2.2.2.2 | Fat Content. The fat content was determined by SE using a Soxtherm apparatus following the methodology reported by Tzompa-Sosa et al. (2014) with some modifications. Briefly, approximately 4 g of tomato pomace was accurately weighed into an extraction thimble. The sample was then extracted with 200 mL of petroleum ether. After extraction, the thimble was left overnight to allow the petroleum ether to evaporate. It was then weighed again on an analytical balance, along with boiling stones and fat, to determine the amount of fat extracted. The analysis was carried out in triplicate.

2.2.3 | Solvent Extraction

The SE was performed following the methodology developed by Sadler et al. (1990). One gram of raw material or raw material processed in various ways as previously described was mixed with 2 mL of Milli-Q water and extracted with 13.5 mL of a hexane–acetone–ethanol mixture in a 2:1:1 ratio (v:v:v). The sample was then mixed with 3.75 mL of water and stirred for 10 min. After stirring, the mixture was centrifuged at 3000 × *g* for 10 min, and the supernatant was removed. This extraction step was repeated at least three times. The nonpolar phase was transferred to a round-bottomed distillation flask and evaporated using a Hei-VAP rotary evaporator (Heidolph, Schwabach, Germany) at 50°C for 5 min. The resulting dry residue was redissolved in 10 mL of a mixture of 80% Eluent A (methanol [MeOH]:methyl *tert*-butyl ether [MTBE] [90:10] with 0.1% BHT [w/v]) and 20% Eluent B (10% MeOH:90% MTBE with 0.1% BHT [w/v]), then filtered through a 0.20 µm Millipore filter to obtain the extract, ready for injection into the chromatographic system. Lycopene extraction was performed under subdued light, and the samples were stored at −80°C to prevent degradation if not analyzed on the same day. The extracts were analyzed and quantified by HPLC. The extraction was carried out in triplicate.

2.2.4 | Supercritical Liquid Fluid CO_2 Extraction

The SFE was performed at FeyeCon Carbon Dioxide Technologies (Weesp, the Netherlands) using a Sitec extractor (Zurich, Switzerland). The cylinder was filled with ±80 g of extraction material divided into three parts, separated by a total of four layers of metal rings to scatter the CO_2 throughout the material. The settings of the apparatus were set to a CO_2 flow of 8 kg/h and an extracting temperature of either 50°C for mild extraction temperature or 90°C for a high extraction temperature. The pressure was maintained constant at 200 bar and the temperature at 36°C throughout all phases. The total extraction time was 90 min. The amount of extract was expressed as the amount of extract product (oleoresin) on the total starting material. The extracts were stored at −20°C until all extracts were collected (maximum of 4 days) and further stored at −80°C to prevent degradation (for ±1.5 months, until further analysis). The extract was then dissolved and diluted with tetrahydrofuran to a concentration of 0.007–0.017 g extract/mL solution to be analyzed by HPLC for lycopene quantification. The extraction was carried out once for each setting.

2.2.5 | Lycopene Quantification

The lycopene quantification was carried out using an HPLC system (WaterCorporation, Milford, MA, USA) equipped with photodiode array detector (PDA), following the methodology reported by Bot et al. (2018). The samples obtained by SE and SFE were analyzed by HPLC in triplicate.

A C30 reverse-phase carotenoid column (250 × 4.6 mm^2, S-5) from YMC Corporation (Waters, Zellik, Belgium) was used by HPLC to quantify lycopene. Two mobile phases were employed: the first (Eluent A) was composed of MeOH and MTBE (90:10) with 0.1% BHT (w/v), whereas the second mobile phase (Eluent B) was composed of MeOH and MTBE (10:90) with 0.1% BHT (w/v). Both eluents were sonicated for 20 min before use.

Eluents A and B were used in a combination of linear gradient and isocratic conditions. The pumps, A (Eluent A) and B (Eluent B), were programmed according to the following sequence (values in %): 0–2 min: 88:12, 2–4 min: 73:27, 4–6 min: 57:43, 6–8 min: 43:57, 8–9.5 min: 20:80, 9.5–15 min: 0:100, 15–25 min: 88:12. The flow rate was 1 mL/min, the injection volume was 20 µL, and the total run time was 25 min.

The separation was carried out with an injection volume of 20 µL, a flow rate of 1 mL/min, and a column temperature set at 25°C. The UV–visible spectrum was obtained within a wavelength range of 300–550 nm, and detection was performed at a wavelength of 476 nm.

A calibration curve was prepared by HPLC, using all-trans-lycopene as a standard, in the range of 1.25–10 µg/mL, to determine the concentration of lycopene in the samples. The calibration curve was applied to both all-*trans*-lycopene and its *cis*-isomers, as the levels of *cis*-isomers are expressed as all-*trans*-lycopene equivalents. The identification of the all-*trans*-lycopene peak in the HPLC chromatograms was confirmed using an all-*trans*-lycopene standard. Peaks corresponding to the *cis*-isomers of lycopene were identified by assigning them on the basis of their retention times and the characteristic UV–Vis spectral shape of lycopene, comparing these results with previously reported data in the literature (Honda et al. 2015; Gupta et al. 2015).

2.2.5.1. Calculation The amount of different lycopene isomers yielded per dry weight of extraction material was calculated using the following equation:

$$\text{Lycopene isomer yield} = \frac{\left(\frac{A}{K}\right) \times m}{\text{dw}} \quad (1)$$

where A is the peak area of isomer; m is the mass of extract (g); K is the calibration curve constant; and dw is the dry weight of tomato extract.

In this formula, the lycopene isomer yield was the amount of an isomer yielded on a dry basis (µg/g dry matter of tomato extract material).

The total lycopene yield and total *cis*-lycopene yield in a sample were calculated as the sum of yields of all lycopene isomers and

all *cis*-lycopene isomer yields in a sample, respectively. The total *cis*-lycopene isomer content (%) in the extracts and the content of each isomer separately (%) were determined from the number of *cis*-lycopene isomers yielded as a percentage of the total amount of lycopene isomers yielded.

2.3 | Statistical Analysis

The results are presented as mean ± standard deviation and were analyzed using IBM SPSS Statistics 28 (IBM, Armonk, USA). A multivariate analysis of variance (MANOVA) was performed to assess the effects of drying, particle size, and thermal pretreatments on SE and the effects of drying, particle size, thermal pretreatments, and extraction temperature on the SFE ($\alpha = 0.05$). The percentage of total variation was calculated to determine the contribution of each factor and the interactions to the overall variance.

3 | Results and Discussion

3.1 | Characterization of Raw Tomato Pomace

The raw tomato pomace, consisting of tomato peels, seeds, and stems before any pretreatment (moisture content: 84.2% ± 1.6%, in line with previously reported data (Del Valle et al. 2006; Silva et al. 2019)), was extracted using SE, and it contains 542 ± 85 μg/g dry matter of lycopene. This value fell within the range reported in previous studies, which ranged from 342 μg/g dry matter (Zuorro et al. 2011) to 2720 μg/g dry matter (Zuorro 2020), both using hexane–acetone–ethanol (2:1:1). The differences found in lycopene content were likely due to several factors. In this study, the unprocessed material included peels but also seeds (which have a lower lycopene content) and small amounts of other residuals like stems and dirt (Lu et al. 2019). Moreover, lycopene content is affected by variables such as growing season, location, cultivar, and maturity, which might have influenced the amount of it inside the tomato peels (Garcia and Barrett 2006). The amount of *cis*-lycopene in the untreated tomato pomace was 20.5% ± 2.9% of the total lycopene, consistent with values reported in the literature for tomato by-products (15%–44%) (Ho et al. 2015).

3.2 | Differently Processed Tomato Pomace Characteristics: Moisture Content and Fat Content

The raw tomato pomace was dried using two methods (i.e., OD and FD), then ground to two particle sizes (i.e., 0.5 and 2 mm), and half of these samples were thermally pretreated. The resulting materials, referred to as tomato pomace extraction material from now on, were characterized in terms of moisture and fat content. The results are presented in Table 1.

The moisture content of the tomato pomace extraction material ranged from 4.4% to 6.7% w/w. The tomato pomace was dried to ensure material stability and prevent physicochemical and microbiological degradation (Silva et al. 2019). The moisture content was primarily influenced by thermal pretreatment (Table S1), which significantly reduced the water content in the material.

The fat content in the tomato pomace extraction material ranged from 6.9% to 8.5% w/w. This variation primarily depends on the particle size (Table S1), as smaller particles facilitate higher fat extraction than larger particles. Previous studies, such as that of Silva et al. (2019), reported fat content values for tomato pomace around 15%. This discrepancy might be attributed to differences in the composition of the starting material, specifically the proportion of seeds versus peels, given that seeds generally have a higher oil content than peels. In the present study, olive oil (~1% w/w dry matter, DM) was added to all materials, both FD and OD, to serve as a cosolvent during SFE and aid in thermal pretreatment (Shi et al. 2009; Watanabe et al. 2018).

3.3 | Lycopene Content of Tomato Pomace Extracted by SE

The yield of lycopene extracted through SE and the *cis*-isomer content (%) of tomato pomace extraction material are summarized in Table 2. The highest lycopene yield, 791 μg/g DM, was achieved by combining FD with a particle size of less than 0.5 mm and thermal pretreatment. In contrast, OD samples with a particle size under 2 mm yielded the lowest amount, at 290 ± 42 μg/g DM. These results highlight that reducing particle size from 2 to 0.5 mm and employing FD significantly enhance lycopene extraction. As supported by MANOVA results (Table S1), particle size had the most substantial effect (SS% 56.7%) on the lycopene yield. Reducing particle size increased the breakdown of cell walls, thereby enhancing the contact surface area available to the solvent, accelerating the extraction, and increasing the yield (Reverchon and De Marco 2006; Sabio et al. 2003).

Regarding isomerization, *cis*-isomer content ranged from 60.9 ± 8.0 μg/g DM (21.0%) for OD, <2 mm to 304.2 ± 13.1 μg/g DM (38.4%) for FD, <0.5 mm-thermally pretreated (TP). Comparing the same sample with and without thermal pretreatment, pretreated samples exhibited nearly double the *cis*-isomer content compared to untreated samples, with a significant role of thermal pretreatment in isomerization ($p < 0.001$, explaining 99.5% of variation). This aligns with previous studies showing that thermal treatments increase isomerization due to the additional energy input, which leads to a geometric change in the conjugated bonds (Honest et al. 2011).

3.4 | Lycopene Content of Oleoresin Obtained by SFE

The SFE extract, a highly pigmented red substance, was identified as oleoresin, a semi-solid oil-based extract formed by the evaporation of the solvent used during extraction (Kehili et al. 2017). Oleoresin was a complex mixture that, in addition to lycopene, contains several other lipophilic phytochemicals, such as other carotenoids, tocopherols, phytosterols, and polyunsaturated fatty acids (Bruno et al. 2018; Lenucci et al. 2010). Oleoresin yield reflects the overall SFE extraction efficiency and, in conjunction with lycopene yield, indicates the overall SFE performance of extracting lycopene from tomato waste. As reported in Table 3, total oleoresin yield varied significantly from 2% w/w extraction material (FD, <0.5 mm-TP-90°C) to 25.6% w/w (FD, <2 mm-TP-50°C). Total lycopene yields also showed a wide range from

TABLE 1 | Moisture content and fat content of tomato pomace.

Sample	Moisture content (% w/w)	Fat content extraction material (% w/w)
FD, <2 mm-TP	4.4 ± 0.2	8.0 ± 0.2
FD, <2 mm	5.7 ± 0.1	7.9 ± 0.2
FD, <0.5 mm-TP	5.3 ± 0.1	8.5 ± 0.2
FD, <0.5 mm	6.4 ± 0.1	8.2 ± 0.2
OD, <2 mm-TP	5.4 ± 0.4	6.9 ± 0.2
OD, <2 mm	6.4 ± 0.2	6.9 ± 0.2
OD, <0.5 mm-TP	5.6 ± 0.4	8.3 ± 0.2
OD, <0.5 mm	6.7 ± 0.1	8.1 ± 0.2

Note: The values are expressed as mean ± standard deviation. Drying methods: FD (freeze-drying) and OD (oven-drying). Particle size: <0.5, <2 mm.
Abbreviation: TP, thermal pretreatment.

TABLE 2 | Total lycopene yield and *cis*-lycopene content of tomato pomace obtained with conventional solvent extraction.

Sample	Total lycopene yield (μg/g DM)	*Cis*-lycopene content (μg/g DM) (% of tot. lyc.)
FD, <2 mm-TP	519.7 ± 40.8	215.3 ± 22.0 (41.4)
FD, <2 mm	488.7 ± 27.3	98.9 ± 3.3 (20.3)
FD, <0.5 mm-TP	791.4 ± 36.4	304.2 ± 13.1 (38.4)
FD, <0.5 mm	687.9 ± 14.0	124.5 ± 14.3 (18.1)
OD, <2 mm-TP	312.7 ± 9.4	120.3 ± 0.6 (38.5)
OD, <2 mm	290.4 ± 41.7	60.9 ± 8.0 (21.0)
OD, <0.5 mm-TP	546.7 ± 30.9	251.4 ± 12.9 (39.4)
OD, <0.5 mm	530.7 ± 26.6	102.7 ± 5.7 (19.4)

Note: The values are expressed as mean ± standard deviation. Drying methods: FD (freeze-drying), OD (oven-drying). Particle size: <0.5, <2 mm.
Abbreviations: DM, dry matter; TP, thermal pretreatment.

TABLE 3 | Oleoresin yield, total lycopene yield, and *cis*-lycopene content of tomato pomace extracted with supercritical fluid.

Samples	Oleoresin yield (% w/w extraction material)	Total lycopene yield (μg/g DM)	*Cis*-lycopene content (μg/g DM) (% of tot. lyc.)
FD, <2 mm-TP-50°C	25.6	n.d.	n.d.
FD, <2 mm-TP-90°C	2.3	52.7 ± 4.5	18.7 ± 1.7 (35.5)
FD, <0.5 mm-TP-50°C	14.3	574.3 ± 11.8	275.9 ± 6.3 (48.6)
FD, <0.5 mm-TP-90°C	2.0	43.7 ± 7.9	23.4 ± 3.4 (53.8)
FD, <2 mm-50°C	5.1	234.9 ± 12.0	88.7 ± 7.7 (37.9)
FD, <0.5 mm-90°C	2.3	54.4 ± 5.3	20.6 ± 1.7 (37.8)
OD, <2 mm-TP-50°C	8.7	299.6 ± 5.4	118.1 ± 2.7 (39.4)
OD, <2 mm-TP-90°C	3.4	39.7 ± 1.2	22.9 ± 0.5 (57.7)
OD, <0.5 mm-TP-50°C	4.2	480.6 ± 11.5	211.8 ± 7.2 (44.0)
OD, <0.5 mm-TP-90°C	3.5	44.3 ± 2.3	25.9 ± 1.6 (58.4)
OD, <2 mm-50°C	6.2	183.2 ± 4.1	51.6 ± 1.7 (28.2)
OD, <0.5 mm-90°C	3.9	60.2 ± 3.0	27.3 ± 1.0 (45.3)

Note: The values are expressed as mean ± standard deviation. Drying methods: FD (freeze-drying), OD (oven-drying). Particle size: <0.5, <2 mm. Extraction temperatures: 50°C and 90°C.
Abbreviations: DM, dry matter; n.d., not detectable; TP, thermal pretreatment.

39.7 μg/g DM (OD, <2 mm-TP-90°C) to 574 μg/g DM (FD, <0.5 mm-TP-50°C). This range is consistent with previously reported values, which span from 15 μg/g DM (extracted at 345 bar, 86°C, stored at −20°C, 30% peels) (Rozzi et al. 2002) to 459 μg/g DM (extracted at 40 MPa, 90°C, ground, drying method unspecified, 37% peels) (Machmudah et al. 2012).

3.4.1 | Effect of Extraction Temperature

The oleoresin and lycopene yields were significantly higher in samples extracted at 50°C than those at 90°C. For instance, the freeze-dried <0.5 mm tomato pomace sample extracted at 50°C (FD, <0.5 mm-TP-50°C) had lycopene yield of 574.3 ± 11.8, which is almost 10 times higher than its counterpart extracted at the higher temperature (FD, <0.5 mm-TP-90°C) (Table 3). Both oleoresin and lycopene yields were significantly affected by extraction temperature ($p < 0.001$), accounting for 85% and 94% of the total variation, respectively (Table S2). The effect of temperature on lycopene extractability is a complex phenomenon because it involves two simultaneous effects. Although higher temperature increases solute vapor pressure, enhancing solubility in CO_2, it also decreases CO_2 density at constant pressure, thus reducing its solvating power (Antonie and Pereira 2019). In the present study, with pressure maintained at 200 bar, the CO_2 density was higher at the lower temperature (~50°C), therefore, consistent with Filho et al. (2008) who observed a decrease in total extraction yield with increasing temperature from 40°C to 60°C at constant pressure (<150 bar), the CO_2 density had a greater influence on oleoresin yield than solute vapor pressure at 200 bar. Furthermore, CO_2 selectivity varies with density. Lower CO_2 density (associated with higher temperatures) favors the solubilization of nonpolar solutes with low MW and high vapor pressure (Antonie and Pereira 2019). Conversely, higher CO_2 density promotes the dissolution of larger, slightly polar, less volatile solutes (Ahmad et al. 2019). This might explain the higher oleoresin yield at lower temperatures, where a wider range of solutes was likely dissolved. Moreover, lycopene has a relatively high MW (536.9 g/mol), and therefore, it was more readily extracted at higher SC–CO_2 densities (lower temperature), which facilitates the dissolution of larger molecules (Shi et al. 2009).

3.4.2 | Effect of Drying Methods

Among samples extracted at 50°C, lycopene yield was 1.19 and 1.28 times higher in freeze-dried samples than OD samples under the same conditions (thermal pretreatment and particle size), as shown in Table 3. On the basis of MANOVA results (Table S2), both oleoresin ($p < 0.05$) and lycopene yields ($p < 0.001$) were significantly affected by the drying methods used before extraction; however, these factors accounted for only 9.7% and 1.2% of the variation, respectively. Strati and Oreopoulou (2016) reported greater lycopene loss in OD samples (70°C for 40 h) due to heat and oxygen exposure, which accelerates degradation compared to FD. Moreover, crystal formation during freezing might have disrupted the plant matrix, facilitating solvent access to the cellular matrix (Sablani et al. 2011). We could not confirm the same trends among the samples extracted at 90°C as the yields were too low to obtain reliable data on the influence of other variables.

3.4.3 | Effect of Particle Size

Decreasing particle size by approximately four times (from 2 to 0.5 mm) led to an approximately 1.6-fold increase in lycopene yield for OD and TP samples, but only among those extracted at 50°C. At 90°C, the high temperature masked the effect of particle size on SFE samples, resulting in very low yields. Therefore, tomato pomace particle size significantly influenced lycopene yield ($p < 0.001$) but explained only 2.8% of the total variation. This demonstrates that reducing particle size within this range effectively increases lycopene yield during SFE, but optimizing other variables, such as extraction temperature, is also necessary. Generally, smaller particle sizes enhance the efficiency of SC–CO_2 extraction. This is primarily due to their higher surface-to-volume ratio, which provides a greater surface area for the SC–CO_2 to interact with the lycopene. Moreover, reducing the particle size of plant materials also destroys cell walls, which naturally act as physical barriers, limiting the diffusion of the lycopene into the SC–CO_2. With disrupted cell walls, the diffusion path for the solvent is shortened, leading to lower internal mass transfer resistance and, consequently, a more effective extraction process (Zuknik et al. 2012; Reverchon and De Marco 2006).

3.4.4 | Effect of Thermal Pretreatment

Lycopene yield was slightly but significantly ($p < 0.001$) affected by the thermal pretreatment, explaining 0.9% of the variation. This effect was observable only in samples extracted at 50°C, OD, and with a 2 mm particle size. For this specific extraction, thermal pretreatment resulted in an approximately 1.63-fold increase in lycopene yield. This agrees with previous research showing that heat treatment (88–120°C) improves lycopene extraction from tomato purée by breaking down cell walls and releasing primarily all-*trans*-lycopene (Dewanto et al. 2002; Shi et al. 2009). It is hypothesized that the applied thermal pretreatment (120°C for 1 h) made the food matrix more accessible for SC–CO_2. The results indicate that the positive effect of thermal pretreatment on total yield outweighed any negative impact of lycopene degradation at the elevated temperature.

3.5 | Formation of Lycopene *Cis*-Isomers During SFE

As reported in Table 3, the percentage of *cis*-isomer content in the SFE extracts varied between 28.2% and 58.4%, and the amount of *cis*-lycopene ranged from 18.7 to 275.9 μg/g DM. The *cis*-isomer content (% of total lycopene) is a valuable measurement, but it should be considered together with the overall yield to draw conclusions about the performance of the extraction variables. In fact, freeze-dried, finely milled material, TP, and extracted at 50°C (FD, <0.5 mm-TP-50°C) yielded the highest *cis*-lycopene yield (275.9 μg/g DM); instead, OD, <0.5 mm-TP-90°C with 25.9 μg/g DM *cis*-lycopene yield had the highest % of *cis*-isomer content (58.9%) of the total lycopene content.

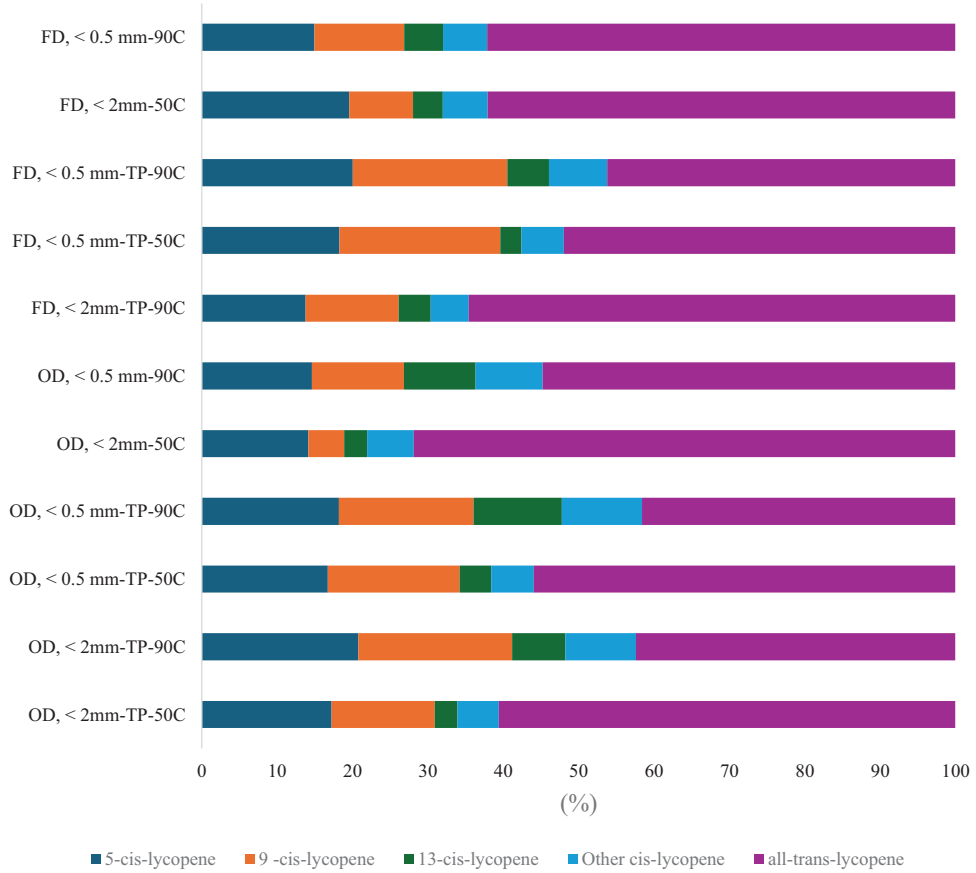

FIGURE 1 | Distribution of lycopene isomers (%) on the total lycopene extracted. Drying methods: FD (freeze-drying), OD (oven-drying). Particle size: <0.5, <2 mm. Extraction temperatures: 50°C and 90°C. n.d.: not detectable; TP, thermal pretreatment.

Regarding *cis*-isomer yields, the thermal pretreatment had the greatest effect ($p < 0.001$), explaining 73.4% of the variance (Table S2), due to the energy input accelerating lycopene isomerization; moreover, higher extraction temperatures favor a higher *cis:trans* ratio. The total *cis*-isomer yield was significantly higher at 50°C, as shown in Table 3. Low yields observed at 90°C could be attributed to degradation due to exposure to high temperatures during processing. It is important to consider that isomerization and degradation are concurrent, competitive processes (Longo et al. 2012) and, under specific conditions, one mechanism may predominate over the other. Interestingly, decreasing the particle size of the raw material also affected isomerization, likely due to the increased surface area that led to a greater energy input throughout all the materials (Reverchon and De Marco 2006). Regarding the influence of drying method, which significantly affected ($p < 0.01$) the isomer composition, no consistent trend was observed between the two drying methods investigated. This contrasts with the results of Strati and Oreopoulou (2016), where OD led to a higher *cis*-isomer content (16% of total lycopene), attributed to isomerization induced by elevated temperature (70°C), compared to FD (9% of total lycopene). The OD temperature in the current study was lower (60°C), which perhaps did not consistently induce significantly higher isomerization compared to FD. This aligns with the statement by Hackett et al. (2004), who mentioned that lycopene may degrade mainly through oxidation without isomerization at 25°C and 50°C. In contrast, isomerization of lycopene in tomato oleoresins increased at 75°C and 100°C.

The specific *cis*-isomer distribution in the SFE extracts was determined. Figure 1 presents the isomer distribution profile of the different extracts. The most abundant identifiable isomers quantified by HPLC in the analyzed extracts were all-*trans*, 5-*cis*, 9-*cis*, and 13-*cis*. "Other *cis*-lycopenes" refers to all integrated peaks of unidentifiable *cis*-isomers with retention times between 13-*cis* and 9-*cis*. As shown in Figure 1, 5-*cis* and 9-*cis* lycopene were the most abundant *cis*-isomers in the SFE extracts. Thermal pretreatment significantly influenced their concentrations, accounting for 63% and 74.5% of the variation, respectively (Table S3).

In contrast, 13-*cis* and the unidentifiable *cis*-lycopene were primarily affected by extraction temperature ($p < 0.001$) and were mostly found in extracts obtained at the higher temperature of 90°C. Generally, 13-*cis* is the most abundant isomer formed during high thermal treatment, likely due to its low rotational barrier facilitating its formation. However, 13-*cis* has lower nutritional relevance than 5-*cis* lycopene because of its instability among *cis*-isomers, whereas 5-*cis* lycopene demonstrates greater stability during storage (Shi et al. 2022). Ideally, isomerization from all-*trans* to stable *cis*-isomers, such as 5-*cis*, is desirable due to their higher bioavailability (Papaioannou et al. 2016). This improved bioavailability is likely due to their shorter chain length, which enhances solubility in bile acid micelles and lipids, reduces their propensity for crystallization, and minimizes their tendency to aggregate (Honest et al. 2011; Murakami et al. 2017).

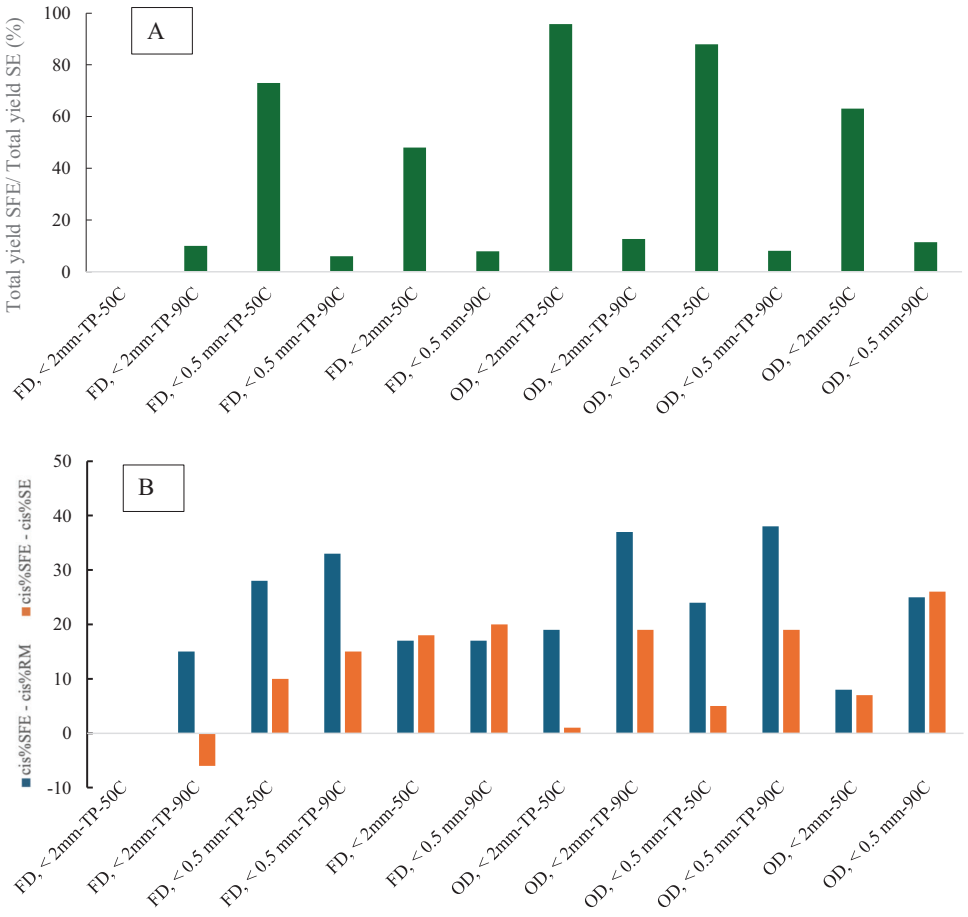

FIGURE 2 | Total lycopene yield obtained using supercritical fluid extraction (SFE) compared to that obtained using solvent extraction (SE) (A); difference in *cis*-isomer content between SFE and raw material (%); and difference in *cis*-isomer content between SFE and SE (%) (B). Drying methods: FD (freeze-drying), OD (oven-drying); particle size: <0.5, <2 mm. Extraction temperatures: 50°C and 90°C. RM, raw material; TP, thermal pretreatment.

3.6 | Efficiency of SFE Compared to SE

The yield of SFE, expressed as a percentage of the SE yield, is shown in Figure 2A. This ratio indicates the effectiveness of SFE in recovering lycopene compared to conventional SE. SE demonstrated higher extractability than SFE. Specifically, SFE at 90°C yielded only a few percent of the SE yield, indicating its inefficiency at this temperature. This aligns with Watanabe et al. (2018), who reported lower lycopene solubility in CO_2 compared to organic solvents. Therefore, optimized pretreatments such as extraction temperature and particle size seemed crucial for SFE to achieve yields comparable to SE. OD, TP material with a particle size smaller than 0.5 mm, extracted at 50°C, achieved a similar yield (close to 96%) of the same type of pretreated material extracted by the conventional SE, as shown in Figure 2A. Despite these improvements, the highest lycopene yield obtained through SFE (574.3 μg/g DM) led to only 72% of the lycopene extracted under the same conditions using SE (791.4 μg/g DM).

To fully evaluate the efficiency of SFE extraction, the isomerization degree should also be considered: The percentage increase in cis-isomer content compared to the raw material (20%) reflects the overall effect of the entire process, encompassing raw material processing (drying, grinding, and thermal pretreatment) and SFE. As shown in Figure 2B, all samples exhibited an increase in cis-isomer content (ranging from +8% to +38%) compared to the raw material. This demonstrates the impact of raw material pretreatment on increasing cis-isomer yield and suggests a higher extractability of cis-isomers through SFE than SE.

The difference in cis-isomer content between SFE and SE (*cis*%SFE–*cis*%SE) highlights explicitly the effect of SFE on cis-isomer content. Except for extract FD, <2 mm-TP-90°C (–6%) and OD, <2 mm-iso-50°C (+1%), cis-isomer content was generally higher after SFE compared to SE. This is interesting when evaluating the advantages of extracting lycopene through SFE: Even if it is less efficient, it might be a better option due to the higher solubilization of the most bioavailable lycopene isomers. Two mechanisms found in the literature can explain this general trend of increased *cis*-isomer content after SFE. One hypothesis suggests that SC–CO_2 preferentially extracts cis-lycopene isomers over all-trans-lycopene (Leone et al. 2010; Watanabe et al. 2018). This implies that cis-isomers have higher solubility in SC–CO_2 than all-trans-lycopene. Another theory proposes that the supercritical CO_2 environment promotes isomerization, facilitating the rotation of conjugated double bonds from all-trans-lycopene to the cis-form (Vallecilla-Yepez and Ciftci 2018).

4 | Conclusion

This study examined the effects of drying method (FD and OD), particle size (<0.5 and <2 mm), a thermal pretreatment (1 h at 120°C), and the extraction temperature (50°C and 90°C) on the lycopene yield obtained through SFE from tomato pomace, as well as the effect of these variables on the *cis*-isomer content.

Extraction temperature is the variable with the greatest effect on lycopene yield, with significantly higher yields for extractions at 50°C compared to those at 90°C. Although the higher temperature (90°C) promoted *cis*-isomerization, the overall *cis*-isomer yield was higher when the extractions were performed at the lower temperatures. Extraction at 50°C is also preferable as it reduces isomerization toward 13-*cis*, the least desirable isomer due to its higher instability than other *cis*-isomers. Reducing particle size effectively increased lycopene yield and was an important factor for maximizing yield. Additionally, applying a thermal pretreatment to the extraction material had a significant effect on *cis*-isomerization. The SFE was conducted at a fixed pressure of 200 bar to maintain mild operating conditions in order to clearly evaluate the impact of the other variables analyzed. Future studies should also explore the effect of varying extraction pressures, with particular attention to their impact on *cis* production as well as lycopene yield.

Although the applied conventional organic SE led to a higher extractability of lycopene than SFE, SFE demonstrated an increased extraction of cis-lycopene isomers. This is attributed to the higher solubility of these isomers in supercritical CO_2 than in conventional organic solvents. This finding highlights the potential of SFE as an environmentally friendly alternative to traditional SE methods, particularly for producing tomato extracts that could be used in the food and pharmaceutical industries, with compositions tailored for health benefits, especially those enriched in cis-lycopene content.

Author Contributions

Marianna Tagliasco: conceptualization, investigation, data curation, validation, visualization, writing – original draft, writing – review and editing. **Kim Neijenhuis**: formal analysis, methodology, data curation, investigation, writing – original draft, writing – review and editing. **Vu Trang Anh Nguyen**: formal analysis, methodology, data curation, investigation, supervision, writing – review and editing. **Nicoletta Pellegrini**: conceptualization, methodology, investigation, supervision, funding acquisition, writing – review and editing. **Vincenzo Fogliano**: conceptualization, methodology, investigation, supervision, funding acquisition, writing – review and editing. All authors have read and approved the final version of the manuscript.

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Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

Data are available from the corresponding author upon reasonable request.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.

Supplementary Material: fft270215-sup-0001-SuppMat.docx