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# Investigation of cyclodextrin as potential carrier for lycopene

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## Abstract

Lycopene is a carotenoid with high antioxidant activity. Numerous studies show its positive effects in the prevention and amelioration of many diseases. However, due to its lack of water solubility, its use is very limited. Developing a formulation with lycopene with favorable therapeutic parameters will allow for a more effective use of this ingredient. The aim of this study was therefore to use supercritical phase extraction to obtain lycopene-containing preparations, and to obtain complexes of the extract with cyclodextrins to improve its solubility and increase its antioxidant potential. Lycopene-containing extracts were obtained by ultrasound-assisted acetone extraction and supercritical phase extraction. The supercritical extract was combined with γ-cyclodextrin, β-cyclodextrin and 2-hydroxypropyl-β-cyclodextrin. Attenuated total reflectance Fourier transform infrared spectroscopy (ATR-FTIR) and X-ray diffraction (XRD) analyses were performed for the obtained systems and extracts. A paddle apparatus was used to evaluate the *in vitro* dissolution, and the samples collected were analysed by HPLC. The antioxidant activity was assessed using the 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical method. The results show that cyclodextrins increase the dissolution of lycopene into an acidic environment and enhance the antioxidant potential of the compound. We conclude that the development of a formulation containing a combination of lycopene obtained by supercritical extraction and cyclodextrin will allow for a wider and more effective use of this ingredient.

**Key words:** lycopene, supercritical phase extraction, cyclodextrins, drug delivery system, antioxidant

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## Introduction

Lycopene is classified as a carotenoid. With other compounds in this group, it is responsible for the red and orange colour of some fruit and vegetables, such as tomato, watermelon, pink grapefruit, guava, apricot, papaya and pumpkin (1, 2). In the human diet, the most common sources of this ingredient are tomatoes and tomato-based products (3). More than 85% of lycopene consumed comes from these sources (4). It is also the cheapest source of this carotenoid (5).

Lycopene shows a high antioxidant potential. It reduces reactive oxygen species and eliminates singlet oxygen, hydrogen peroxide, hydroxyl radicals and nitrogen dioxide (6, 7). It has three main impacts on reactive oxygen species: electron transfer, radical attachment and allylic hydrogen abstraction (6). Lycopene has the ability to increase the levels of enzymatic antioxidants such as catalase, glutathione peroxidase and superoxide dismutase (8). It is also capable of regenerating non-enzymatic antioxidants such as vitamin E and C. These actions have a positive effect on the cellular antioxidant defence system (7). The antioxidant activity of lycopene contributes to the protection of important structures in the human body, such as lipids and DNA (9). Its chemical structure is responsible for its antioxidant activity (10). Its molecule is a linear hydrocarbon with the molecular formula $C_{40}H_{56}$. It contains 2 unconjugated and 11 conjugated double bonds (11).

The solubility of lycopene is influenced by its acyclic structure (11). This carotenoid is insoluble in water (12).

Lycopene shows broad biological activity. Numerous studies show its positive effects in the prevention and amelioration of many diseases (3, 13). There is growing evidence that it has beneficial effects in cardiovascular disease, cancer, diabetes, liver disease, neurological diseases and other disorders (1, 14).

Nowadays lycopene is used in the pharmaceutical, food and cosmetic industries due to its beneficial effects (2). However, due to the presence of unsaturated bonds in its molecule, it is highly unstable and sensitive to external conditions such as oxygen, heat, light, acids and metal ions (2, 15, 16). The poor stability of lycopene and the fact that it is insoluble in water affect its low bioavailability (17). All these factors mean that the antioxidant activity of lycopene cannot be fully exploited and its use is severely limited (2, 17). Developing a formulation with lycopene with favorable therapeutic parameters will allow for greater and more effective use of this ingredient.

Many lycopene extracts available on the market are produced by extraction using organic solvents, which may have adverse effects on the human body and the environment. An alternative solution may be to use extraction in the supercritical phase (18). Supercritical carbon dioxide ($scCO_2$) is one of the most commonly used solvents in this method. This is due to its low critical point (31.2 °C, 7.4 MPa), lack of toxicity, low cost and non-flammability (19). The lower temperatures required for this type of extraction may be beneficial for heat-sensitive compounds (20). Among these types of compounds we can include lycopene (2).

The literature points to various ways of improving the physicochemical properties of lycopene. One of these is to combine it with cyclodextrins (15). Cyclodextrins (CDs) are ring-shaped molecules with a hollow cylindrical structure inside. The inner cavity is hydrophobic and the outer surface is hydrophilic. Cyclodextrins have the ability to form inclusion complexes with the guest molecule and consequently improve its stability and solubility in water (2).

The aim of this study was to use supercritical phase extraction to obtain lycopene-containing preparations, and to obtain complexes of the extract with cyclodextrins to improve its solubility and increase its antioxidant potential.

## Materials and methods

### Materials

Tomato powder, consisting of tomato powder (min. 99%) and anti-caking agent $SiO_2$ (min. 1%), supplied by MIGOgroup, was used in the study. Demineralized water was obtained with the Direct-Q 3 UV water purification system (Merck Millipore). Dimethylsulphoxide (DMSO), methanol, acetone and L(+)-ascorbic acid were purchased from POCH (Gliwice, Poland). DPPH (2,2-diphenyl-1-picrylhydrazine) and β-cyclodextrin were obtained from Sigma-Aldrich (St. Louis, MO, USA). (2-Hydroxypropyl)-β-cyclodextrin was from Sigma-Aldrich (Slovakia). γ-cyclodextrin was purchased from Sigma-Aldrich, Wacker Chemie AG (Burghausen, Germany).

### Performing an ultrasound-assisted acetone extraction

An ultrasound-assisted acetone extraction was carried out to obtain the reference extract. 50 ml of acetone was added to a conical flask containing 10 g of tomato powder. The flasks were then placed in an ultrasonic bath for 20 min at 40 °C. The resulting extract was filtered using a filter. The process was repeated 4 times, each time adding a fresh aliquot of 50 ml of the solvent to the separated powder. The extracts were evaporated to dryness using a vacuum evaporator, then transferred to an Eppendorf-type test tube and stored in the refrigerator.

### Performing extraction in the supercritical phase

The test material was weighed into the extraction vessel and then sealed. The extraction process was performed for about 30 min under 4000 PSI at 40 °C. The process was carried out for about 30 minutes by pumping 250 $cm^3$ of supercritical $CO_2$ through the raw material. The resulting extract was transferred to an Eppendorf-type tube and stored in a refrigerator.

## Preparation of a lycopene system with selected cyclodextrins

### Combination of lycopene-containing extract with γ-cyclodextrin

A combination containing 99.5 mg of supercritical extract and 150.7 mg of γ-cyclodextrin was weighed, yielding a weight ratio of 1:1.5. The mixture was grinded for

6.5 hours in an agate mortar until a homogeneous powder was obtained. The powder was transferred to an Eppendorf tube and stored in a refrigerator.

### Combination of lycopene-containing extract with β-cyclodextrin

A combination containing 100.1 mg of supercritical extract and 148.9 mg of β-cyclodextrin was weighed, yielding a weight ratio of 1:1.5. The mixture was grinded for 5 hours in an agate mortar until a homogeneous powder was obtained. The powder was transferred to an Eppendorf tube and stored in a refrigerator.

### Combination of lycopene-containing extract with 2-hydroxypropyl-β-cyclodextrin

A combination containing 100.5 mg of supercritical extract and 150.2 mg of 2-hydroxypropyl-β-cyclodextrin was weighed, yielding a weight ratio of 1:1.5. The mixture was grinded for 5 hours in an agate mortar until a homogeneous powder was obtained. The powder was transferred to an Eppendorf tube and stored in the refrigerator.

### Analysis of the completed systems using ATR-FTIR

The study was carried out using a Shimadzu IRTracer-100 spectrometer and QATR-10 extended range diamond.

### XRD analysis

The study was performed using a Panalytical Empyrean X-ray diffractometer (Almelo, the Netherlands) with a copper anode (CuKα-1.54 Å).

The analysis was conducted in Brag-Brentano reflection mode with 45 kV and 40 mA parameters. The measurement was carried out in the 3-60° (45 s for each 0.05°).

## *In vitro* dissolution studies of lycopene in combination with cyclodextrins

### HPLC method

A high-performance liquid chromatography (HPLC) method developed by Olives Barba et al. was used to confirm the identity and determine lycopene content (21). Analysis was carried out for samples containing a combination of supercritical extract and cyclodextrins.

**Table I** Chromatographic separation parameters
**Tabela I** Parametri hromatografskog razdvajanja

| | |
|---|---|
| Apparatus | Dionex Ultimate 3000 (Sunnyvale, CA, USA) |
| Column | lBondapack C18 (300mm x 2mm) |
| Mobile phase | Methanol/acetonitrile (90:10 v/v) + triethylamine 0.9 µM The solution was filtered through a 0.45 µm pore size membrane and degassed using ultrasound. |
| Flow rate | 0.9 ml/min |
| Detector | Detector UV |
| Wavelength | 475 nm |
| Injection volume | 10 µl |
| Column temperature | 30 °C |
| Measurement time | 10 minutes |

### *In vitro* dissolution studies

The study was carried out using the ERWEKA DH 1520 release test apparatus. 4.5 mg of extract or prepared mixture was weighed into five gelatine capsules. The capsules were placed in a paddle apparatus. The test was carried out at 36.8 °C, for 90 minutes, at a stirring speed of 50 rpm. The dissolution medium was 0.1 mol/L hydrochloric acid.

5 ml each of extraction solution was taken at intervals of 5, 10, 15, 30, 45, 60 and 90 minutes. Each collected sample was prepared for measurement by HPLC.

5 repetitions were performed. The volume of the dissolution medium was 500 ml.

## Determination of antioxidant activity using the DPPH radical

### Preparation of 0.2 mM DPPH solution

7.8 mg of DPPH was weighed into a 100.0 ml conical flask tightly wrapped in aluminium foil and made up with methanol. The tightly sealed flask was shaken for 45 minutes and then stored in a refrigerator without light.

### Preparation of ascorbic acid solution

20.0 mg of ascorbic acid was weighed into a tightly wrapped aluminium foil 5 ml volumetric flask and made up with distilled water. In aluminium foil-protected Eppendorf tubes, solutions were prepared to make a standard curve with concentrations; 0.12 mg/ml (30 µl stock solution and 970 µl distilled water), 0.06 mg/ml, 0.03 mg/ml, 0.015 mg/ml (by 1:1 dilutions).

**Preparation of acetone extract solution**

5 mg of dry extract was weighed and dissolved in 1 ml of DMSO to obtain a solution of 5.0 mg/ml. The whole mixture was stirred to dissolve completely. Subsequently, further dilutions were prepared by 1:1 dilutions: 2.5 mg/ml, 1.25 mg/ml and 0.625 mg/ml.

**Preparation of the supercritical extract solution**

3 mg of dry extract was weighed and dissolved in 1 ml of DMSO to obtain a solution of 3.0 mg/ml. The whole mixture was stirred to dissolve completely. Dissolution was assisted by ultrasonication and a temperature of 37 °C in a water bath. Subsequently, further dilutions were prepared through 1:1 dilutions: 1.5 mg/ml, 0.75 mg/ml and 0.375 mg/ml.

**Preparation of a solution of lycopene-cyclodextrin complex**

5 mg of lycopene-cyclodextrin complex was weighed and dissolved in 1 ml of DMSO to obtain a solution of 2.0 mg/ml. The sample was mixed to dissolve the complex completely. Dissolution was assisted by ultrasound and temperature of 37 °C in a water bath. Subsequently, further dilutions were prepared through 1:1 dilutions: 1.0 mg/ml, 0.5 mg/ml and 0.25 mg/ml.

**Procedure for the determination of antioxidant activity**

25.0 µl of test sample or standard substance and 175 µl of DPPH solution were applied to the plate. The blank was 25 µl DMSO or water and 175 µl methanol, and the control was 25 µl DMSO and 175 µl DPPH reagent. The plate was wrapped tightly in aluminium foil and shaken for 5 minutes at 25 °C and then incubated for 25 minutes at room temperature. Absorbance was measured at 517 nm using a Thermo Scientific Multiskan GO plate reader.

Antioxidant activity was determined by the formula:

$$\text{DPPH scavenging activity (\%)} \left[\frac{Ao - Ai}{Ao}\right] \times 100\%$$

where: $A_o$ - absorbance of the control sample - absorbance of the sample background, $A_i$ - absorbance of the test sample - absorbance of the sample background.

The $EC_{50}$ value for the test substance, which corresponds to an antioxidant concentration capable of neutralising 50% of the radicals, was determined. For this purpose, the dependence of the antioxidant concentration on the reducing capacity of the DPPH radical was plotted.

## Results

### Analysis of the completed systems using ATR-FTIR

FT-IR analysis was used to confirm the interactions between the extract and cyclodextrin (γ-CD, β-CD and 2-HP-β-CD) in the obtained systems.

The spectra of pure samples ($CO_2$ extract, cyclodextrin) were compared with the physical mixture and the obtained system.

The spectra of the physical mixtures are entirely obscured by cyclodextrin (Figure 1-3, blue lines). There are no band shifts that would indicate the interaction of cyclodextrin with the extract. However, changes like the spectra are observed in the ranges of the systems (Figure 1-3, green lines). Changes in the FT-IR spectra that may indicate an interaction between the $CO_2$ extract and cyclodextrin are marked with a rectangular frame in the figures.

For the extract + γ-CD system (Figure 1, green line), band shifts are visible at 1152 $cm^{-1}$ → 1153 $cm^{-1}$, 2928 $cm^{-1}$ → 2926 $cm^{-1}$ and 3316 $cm^{-1}$ → 3325 $cm^{-1}$.

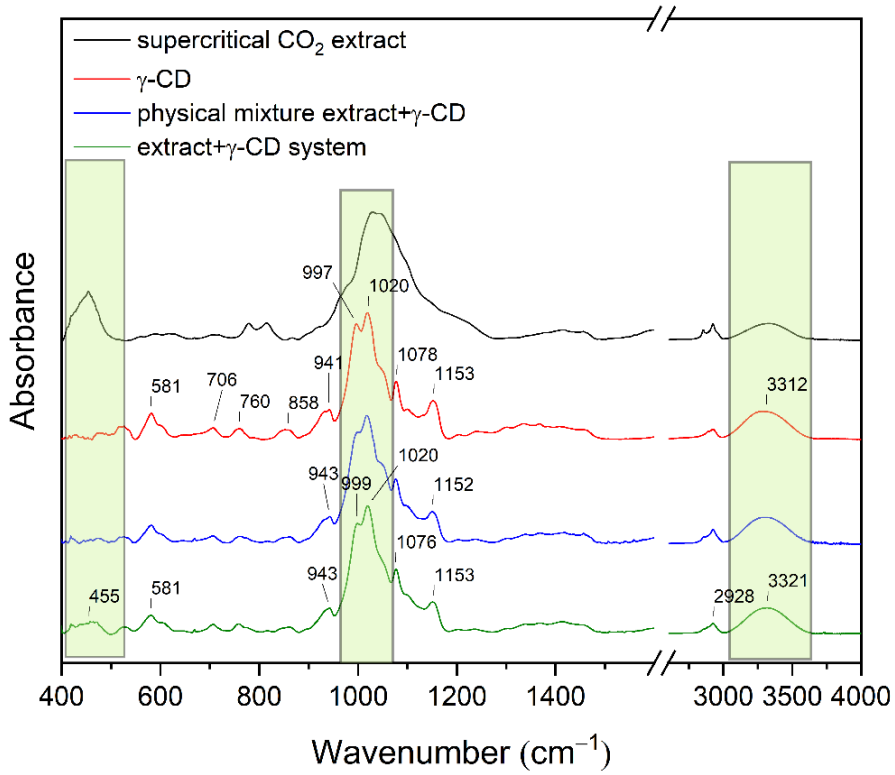


**Figure 1.** **FT-IR analysis: (a) supercritical $CO_2$ extract (black line), γ-cyclodextrin (γ-CD, red line), physical mixture extract+γ-cyclodextrin (blue line), extract+γ-cyclodextrin system (green line)**

**Slika 1.** **FT-IR analiza: (a) superkritični $CO_2$ ekstrakt (crna linija), γ-ciklodekstrin (γ-CD, crvena linija), fizička smeša ekstrakt+γ-ciklodekstrin (plava linija), ekstrakt+γ-ciklodekstrin sistem (zelena linija)**

For the extract + β-CD system (Figure 2, green line), the changes involve bands at: 577 $cm^{-1}$ → 575 $cm^{-1}$, 606 $cm^{-1}$ → 608 $cm^{-1}$, 1020 $cm^{-1}$ → 1022 $cm^{-1}$, 2853 $cm^{-1}$ extract → band disappearance in the system. The band at about 453 $cm^{-1}$, characteristic of the extract in the system spectrum, has an altered shape, reduced intensity, and is shifted to 461 cm-1.

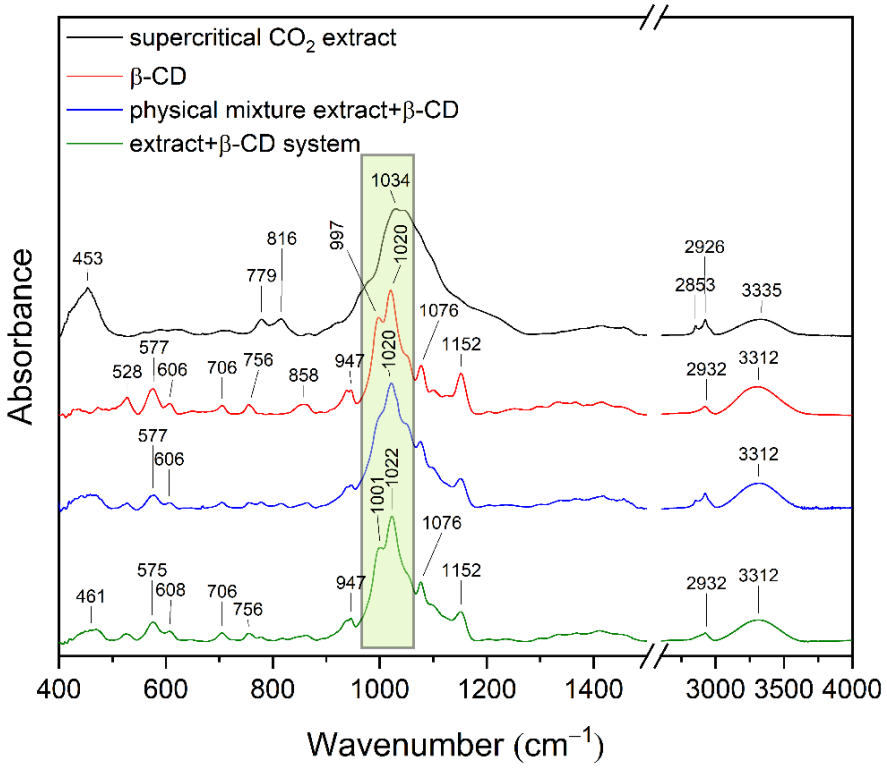


**Figure 2. FT-IR analysis: $CO_2$ supercritical extract (black line), β-cyclodextrin (β-CD red line), physical mixture extract + β-cyclodextrin (blue line), extract + β-cyclodextrin system (green line)**

**Slika 2. FT-IR analiza: $CO_2$ superkritični ekstrakt (crna linija), β-ciklodekstrin (β-CD crvena linija), ekstrakt fizičke smeše + β-ciklodekstrin (plava linija), ekstrakt + β-ciklodekstrin sistem (zelena linija)**

A similar situation occurs for the extract + 2-HP-β-CD system (Figure 3, green line). The extract-derived band (453 $cm^{-1}$) is also seen at 461 $cm^{-1}$. A shift in the bands characteristic of 2-HP-β-CD occurs for bands at 851 $cm^{-1}$ → 856 $cm^{-1}$, 1020 $cm^{-1}$ → 1026 $cm^{-1}$, 3356 $cm^{-1}$ → 3346 $cm^{-1}$.

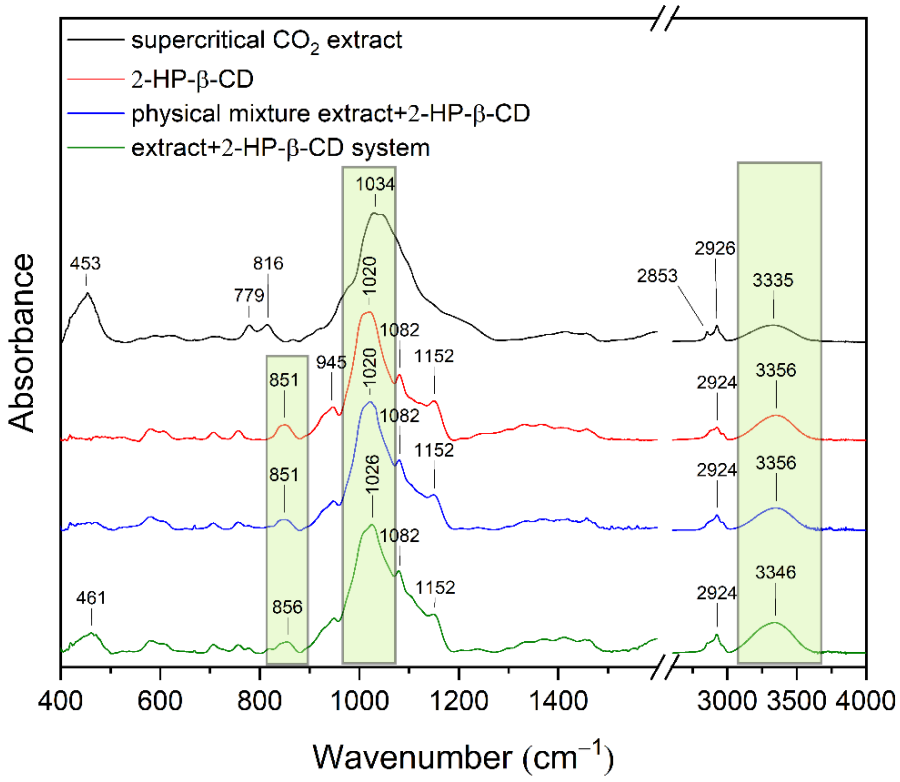


**Figure 3. FT-IR analysis: $CO_2$ supercritical extract (black line), 2-HP-β-cyclodextrin (red line), physical mixture extract+2-HP-β-cyclodextrin (blue line), extract+2-HP-β-cyclodextrin system (green line)**

**Slika 3. FT-IR analiza; $CO_2$ superkritični ekstrakt (crna linija), 2-HP-β-ciklodekstrin (crvena linija), ekstrakt fizičke smeše+2-HP-β-ciklodekstrin (plava linija), ekstrakt+2-HP-β-ciklodekstrin sistem (zelena linija)**

### XRD analysis

X-ray diffraction was used to confirm the structure of the studied samples and the formation of possible interactions between tomato powder and cyclodextrins.

Diffractometric images of tomato powder (before and after the extraction process with supercritical $CO_2$), individual cyclodextrins and supercritical extract-cyclodextrin systems (after the mashing process) were compared.

The effect of the extraction process using supercritical $CO_2$ on the pure tomato powder sample was tested. In the tomato powder sample tested, we observe a broad peak with maxima at 18.8 and 21.4° 2Θ (Figure 4, red line). After the extraction process with supercritical $CO_2$, we observe only one maximum at about 20.1° 2Θ (Figure 4, blue line).

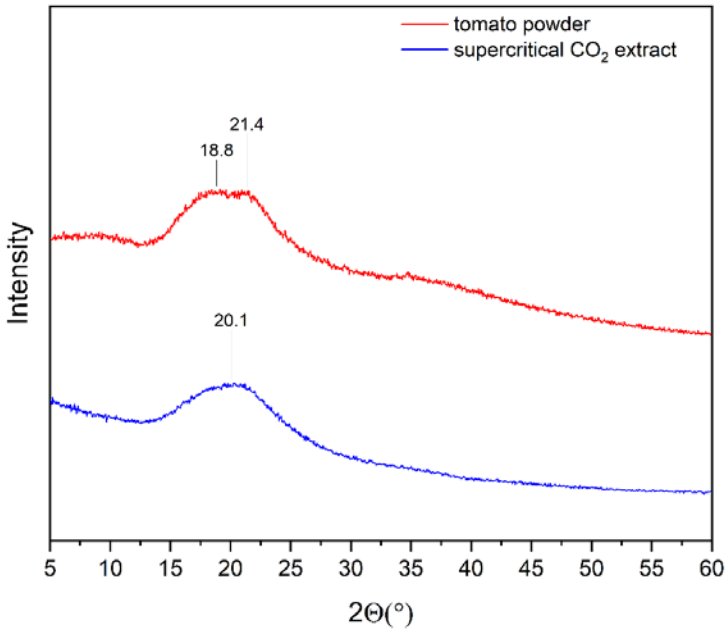


**Figure 4.** **The diffractogram of tomato powder (red line) and tomato powder extract after the supercritical $CO_2$ extraction process**

**Slika 4.** **Difraktogram praha paradajza (crvena linija) i ekstrakta paradajza u prahu nakon superkritičnog procesa ekstrakcije $CO_2$**

In order to confirm or exclude the formation of inclusion complexes, the diffractograms of the extract-cyclodextrin systems obtained by the blotting method were compared with the diffractograms of pure substances and their physical mixtures.

The diffractogram of pure β-cyclodextrin (Figure 5, red line) is characterised by numerous sharp reflections in the range 5-40° 2Θ (so-called Bragg peaks), which confirm its crystalline nature.

In the diffractogram of the extract, there is a broad peak with a maximum at about 19.8° 2Θ (Figure 5, black line), which in the diffractogram of the extract-β-CD system is shifted to 18.8° 2Θ and has an altered shape (Figure 5, green line). In addition, Bragg peaks are absent on the diffractogram of the extract-β-CD system (Figure 5, green line) and are characteristic of β-CD (Figure 5, red line) and present on the diffractogram of the physical mixture (Figure 5, blue line).

HP-β-CD is characterised by two broad reflections with maxima at approximately 10° 2Θ and 19° 2Θ (Figure 6, red line). The physical mixture extract + HP-β-CD retains the character observed for HP-β-CD (Figure 6, blue line). However, a decrease in the intensity of the reflectance at 10° 2Θ is observed. After the run-off process, the diffractogram is not significantly different from that obtained for the physical mixture (Figure 8, green line). The sharp peak observed at about 18.0° 2Θ comes from the shim used during the measurement.

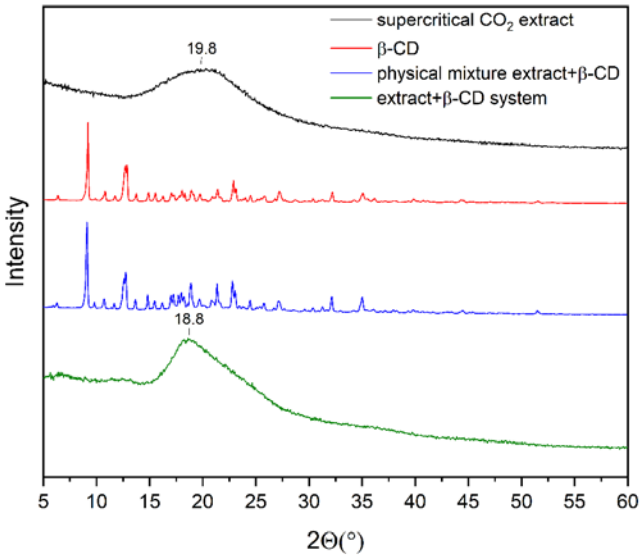


**Figure 5.** **The diffractogram of tomato powder extract after supercritical $CO_2$ extraction (black line), pure β-cyclodextrin (red line), physical mixture extract+β-cyclodextrin (blue line), extract+β-cyclodextrin system (green line)**

**Slika 5.** **Difraktogram ekstrakta praha paradajza nakon superkritične ekstrakcije $CO_2$ (crna linija), čisti β-ciklodekstrin (crvena linija), fizička smeša ekstrakt+β-ciklodekstrin (plava linija), ekstrakt+β-ciklodekstrin sistem (zelena linija)**

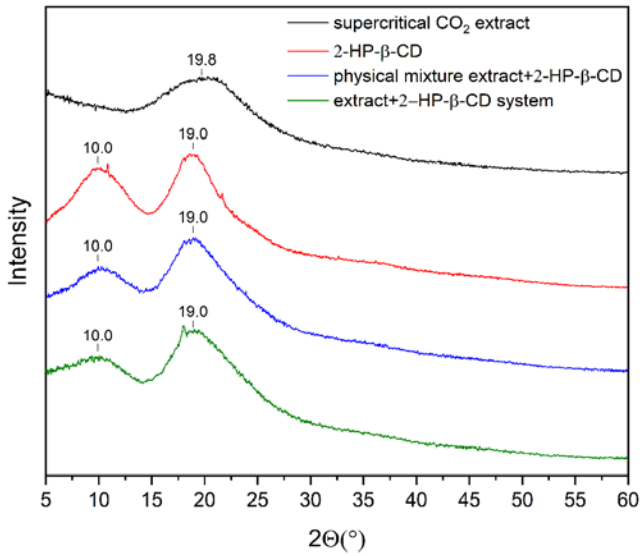


**Figure 6.** **The diffractogram of tomato powder extract after supercritical $CO_2$ extraction (black line), pure 2-HP-β-cyclodextrin (red line), physical mixture extract+2-HP-β-cyclodextrin (blue line), extract+2-HP-β-cyclodextrin system (green line)**

**Slika 6.** **Difraktogram ekstrakta praha paradajza nakon superkritične ekstrakcije $CO_2$ (crna linija), čisti 2-HP-β-ciklodekstrin (crvena linija), ekstrakt fizičke smeše+2-HP-β-ciklodekstrin (plava linija), ekstrakt+2-HP-β-ciklodekstrinski sistem (zelena linija)**

γ-Cyclodextrin also occurs in crystalline form (Figure 7, red line).

The physical mixture extract + γ-CD (Figure 7, blue line) in its course has characteristic Bragg peaks corresponding to pure γ-CD. For the system obtained after the mashing process (Figure 7, green line), we observe changes in the intensity of the reflections corresponding to pure γ-CD.

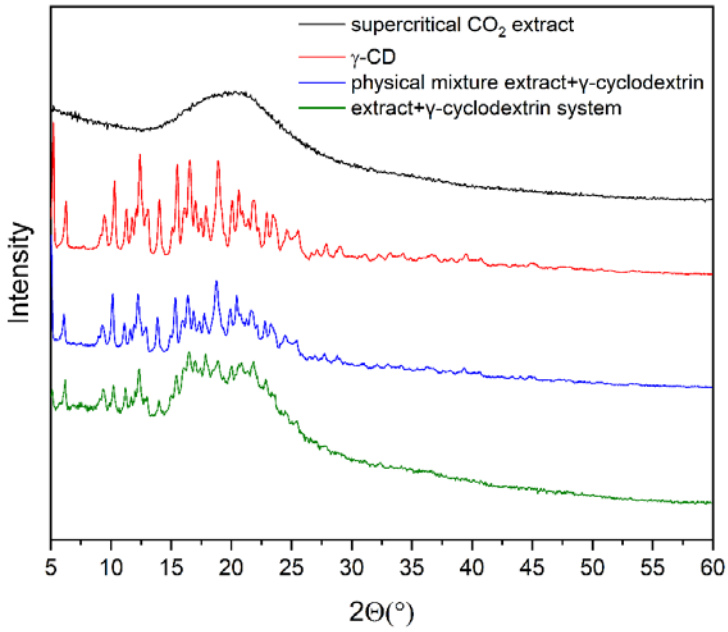


**Figure 7.** **The diffractogram of tomato powder extract after supercritical $CO_2$ extraction (black line), pure γ-cyclodextrin (red line), physical mixture extract+γ-cyclodextrin (blue line), extract+γ-cyclodextrin system (green line)**

**Slika 7.** **Difraktogram ekstrakta praha paradajza nakon superkritične ekstrakcije $CO_2$ (crna linija), čisti γ-ciklodekstrin (crvena linija), fizička smeša ekstrakt+γ-ciklodekstrin (plava linija), ekstrakt + γ-ciklodekstrin sistem (zelena linija)**

### *In vitro* dissolution studies

The aim of the study was to evaluate the effect of the method of extract preparation and the combinations with selected cyclodextrins on the dissolution of lycopene. Following a series of measurements by HPLC, calculations and graphs were made (Figure 8-12).

The study showed that the extracted lycopene is practically not dissolved in an acidic environment (1%). Only when it was combined with cyclodextrins was an improved *in vitro* dissolution in 0,1 M HCl observed. All cyclodextrins showed similar effects on the profile shape and dissolution rate of lycopene. The highest percentage of dissolved API was observed with the lycopene-2-hydroxypropyl-β-cyclodextrin system. This combination increased the dissolution of this compound from 1% to 72%. With the β-cyclodextrin system, an improvement in dissolution of up to 35% was observed, while with γ-cyclodextrin an improvement of up to 68% was observed.

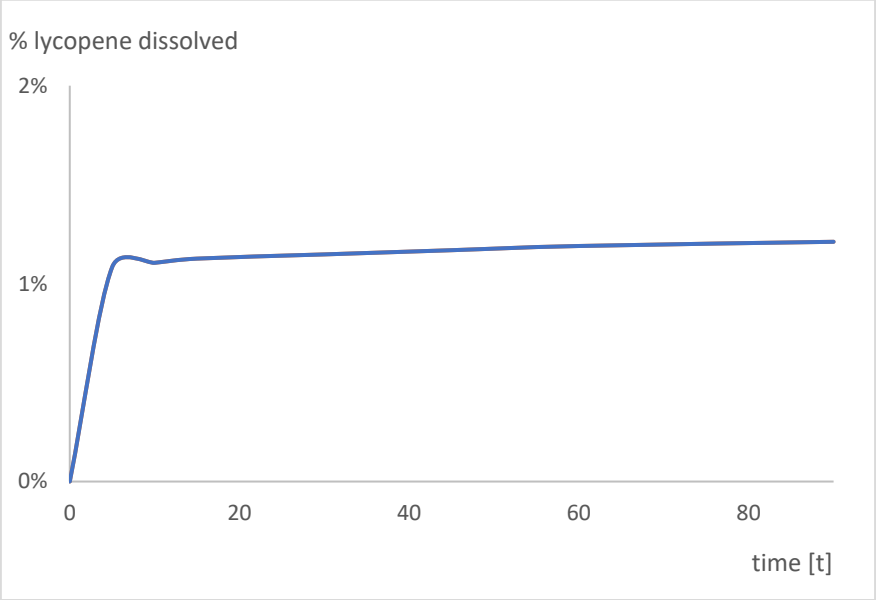


**Figure 8. Percentage of dissolved lycopene obtained by acetone extraction per unit of time**

**Slika 8. Procenat rastvorenog likopena dobijen ekstrakcijom acetona po jedinici vremena**

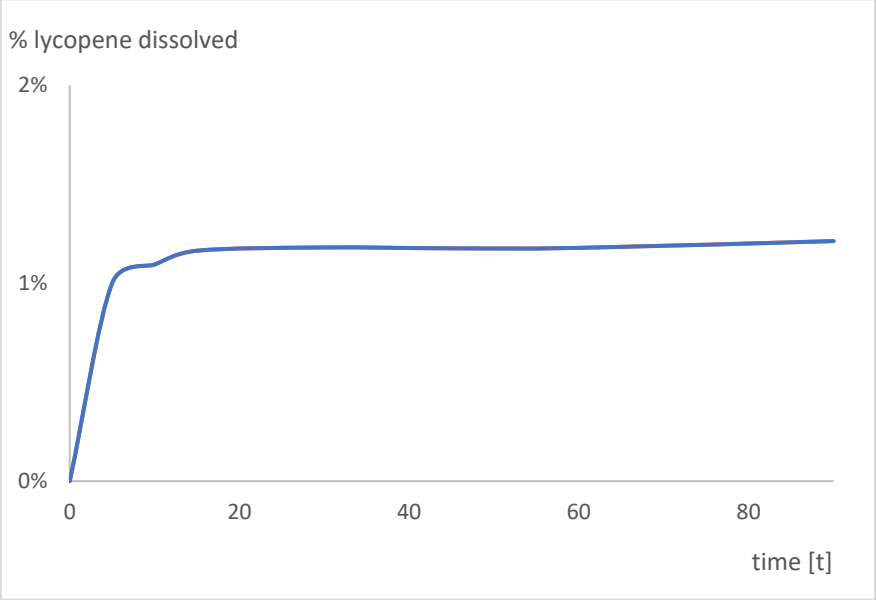


**Figure 9. Percentage of dissolved lycopene obtained by supercritical extraction per unit of time**

**Slika 9. Procenat rastvorenog likopena dobijen ekstrakcijom superkritičnom tečnošću po jedinici vremena**

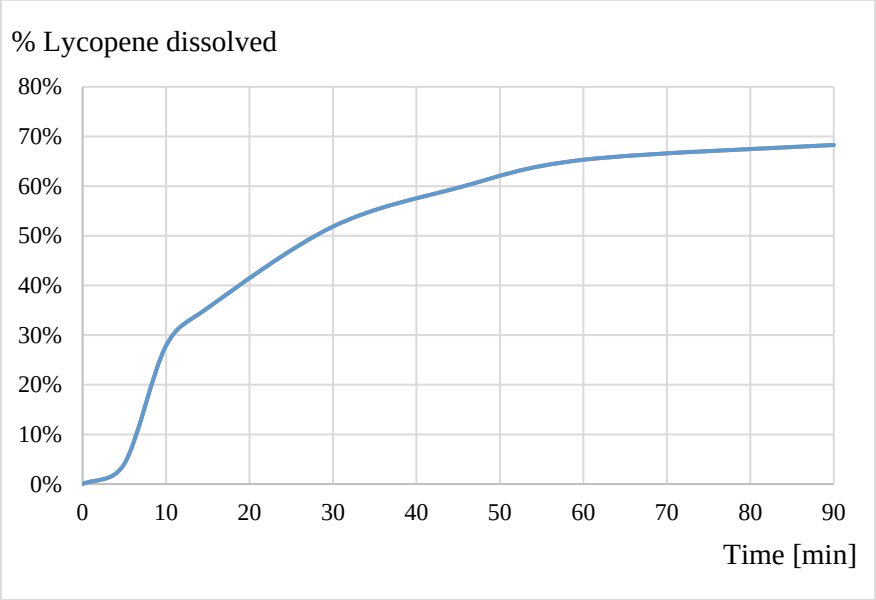


**Figure 10.** **Percentage of lycopene dissolved from the lycopene-γ-cyclodextrin system per unit of time**

**Slika 10.** **Procenat likopena rastvorenog iz sistema likopen-γ-ciklodekstrin po jedinici vremena**

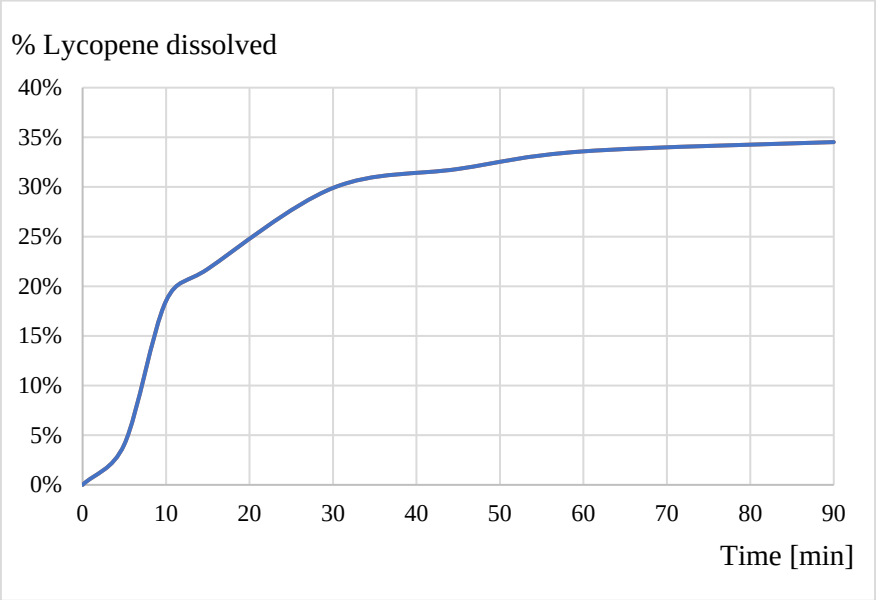


**Figure 11.** **Percentage of lycopene dissolved from the lycopene-β-cyclodextrin system per unit of time**

**Slika 11.** **Procenat likopena rastvorenog iz sistema likopen-β-ciklodekstrin po jedinici vremena**

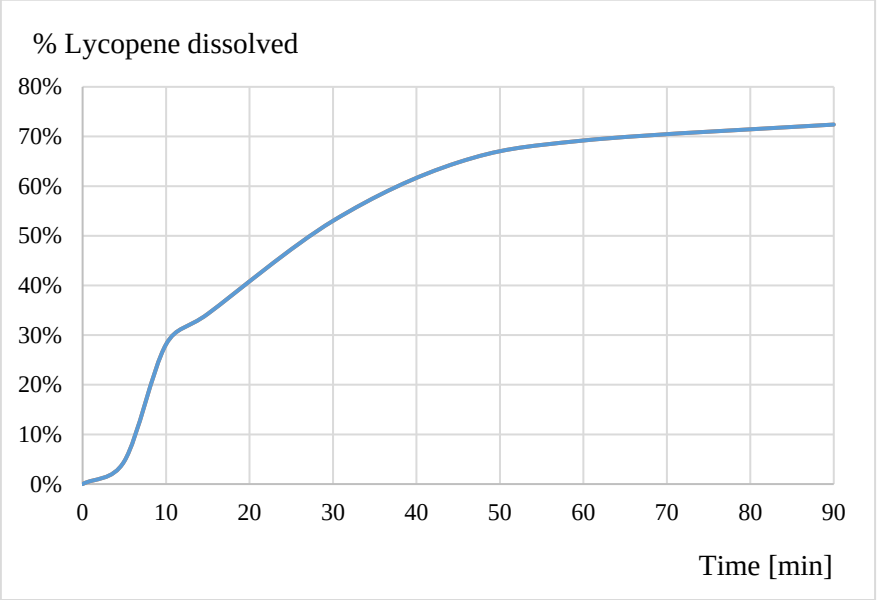


**Figure 12. Percentage of lycopene dissolved from the lycopene-2-hydroxypropyl-β-cyclodextrin system per unit of time.**

**Slika 12. Procenat likopena rastvorenog iz likopen-2-hidroksipropil-β-ciklodekstrinskog sistema u jedinici vremena**

## Determination of antioxidant activity using the DPPH radical

**Table II** Results of studies on the antioxidant activity of ascorbic acid

**Tabela II** Rezultati studija o antioksidativnoj aktivnosti askorbinske kiseline

| Test concentration in the sample [mg/ml] | 0.00188 | 0.00375 | 0.00750 | 0.0150 |
|---|---|---|---|---|
| **DPPH radical scavenging activity [%]** | 12.7 | 21.0 | 52.9 | 92.4 |
| | 10.9 | 23.6 | 49.8 | 92.2 |
| | 10.7 | 24.6 | 52.5 | 93.0 |
| | 9.67 | 19.5 | 56.1 | 92.1 |
| | 12.9 | 20.5 | 53.0 | 93.1 |
| | 13.0 | 23.8 | 51.9 | 92.9 |
| Average activity value | 11.6 | 22.1 | 52.7 | 92.6 |
| Standard deviation | 1.40 | 2.10 | 2.07 | 0.451 |
| Coefficient of variation | 0.120 | 0.0948 | 0.0393 | 0.00480 |
| **$EC_{50}$ [mg/ml]** | **0.00787** | | | |

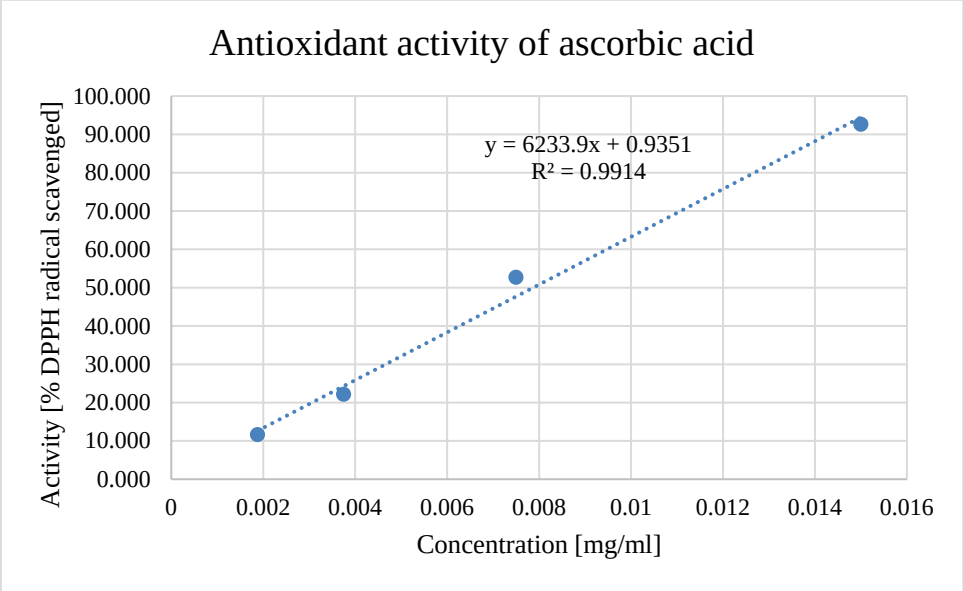


**Figure 13. Chart of the antioxidant activity of ascorbic acid**
**Slika 13. Grafički prikaz antioksidativne aktivnosti askorbinske kiseline**

**Table III** Results of tests on the antioxidant activity of acetone extract
**Tabela III** Rezultati ispitivanja antioksidativne aktivnosti acetonskog ekstrakta

| | | | | |
|---|---|---|---|---|
| Test concentration in the sample [mg/ml] | 0.625 | 1.25 | 2.50 | 5.00 |
| **DPPH radical scavenging activity [%]** | 8.13 | 10.1 | 16.4 | 33.5 |
| | 9.84 | 9.23 | 18.1 | 37.4 |
| | 10.5 | 13.9 | 19.9 | 39.8 |
| | 11.1 | 10.1 | 19.1 | 38.5 |
| | 9.44 | 13.0 | 19.1 | 39.6 |
| | 15.4 | 14.3 | 21.1 | 40.0 |
| | 13.3 | 17.0 | 23.1 | 39.3 |
| | 15.2 | 19.6 | 19.1 | 39.7 |
| Average activity value | 11.6 | 13.4 | 19.5 | 38.5 |
| Standard deviation | 2.70 | 3.61 | 2.00 | 2.16 |
| Coefficient of variation | 0.232 | 0.2694 | 0.1028 | 0.0562 |
| **$EC_{50}$ [mg/ml]** | **7.00** | | | |

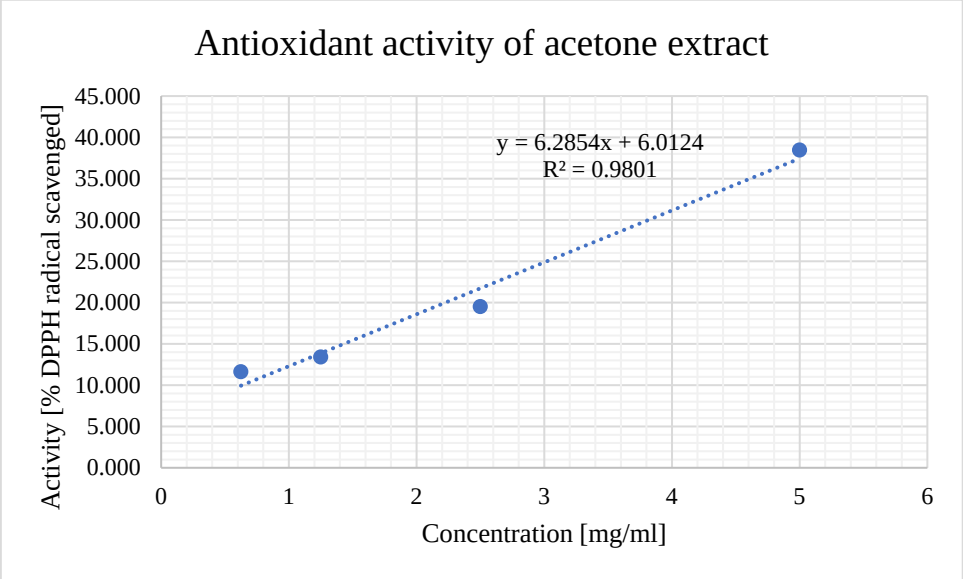


**Figure 14. Chart of the antioxidant activity of acetone extract**

**Slika 14. Grafički prikaz antioksidativne aktivnosti acetonskog ekstrakta**

**Table IV** Results of studies on the antioxidant activity of the supercritical extract

**Tabela IV** Rezultati istraživanja antioksidativne aktivnosti superkritičnog ekstrakta

| Test concentration in the sample [mg/ml] | 0.375 | 0.750 | 1.50 | 3.00 |
|---|---|---|---|---|
| **DPPH radical scavenging activity [%]** | 9.63 | 11.7 | 7.85 | 18.8 |
| | 5.78 | 11.1 | 10.7 | 19.3 |
| | 8.44 | 9.63 | 11.9 | 18.2 |
| | 8.15 | 8.89 | 10.5 | 20.0 |
| | 6.52 | 15.4 | 10.2 | 19.3 |
| | 5.63 | 2.82 | 11.1 | 18.7 |
| | 1.78 | 4.44 | 10.8 | 17.8 |
| | 6.22 | 3.85 | 12.1 | 18.1 |
| Average activity value | 6.52 | 8.48 | 10.6 | 18.8 |
| Standard deviation | 2.39 | 4.42 | 1.31 | 0.734 |
| Coefficient of variation | 0.366 | 0.521 | 0.123 | 0.0391 |
| **$EC_{50}$ [mg/ml]** | **9.86** | | | |

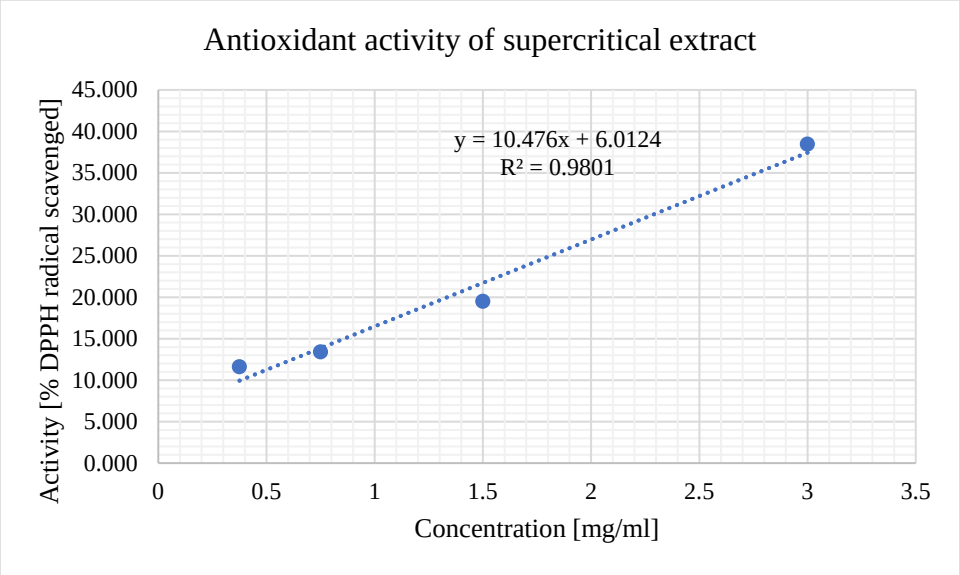


**Figure 15. Chart of the antioxidant activity of the supercritical extract**
**Slika 15. Grafički prikaz antioksidativne aktivnosti superkritičnog ekstrakta**

**Table V** Results of the antioxidant activity of the lycopene - γ-cyclodextrin system
**Tabela V** Rezultati antioksidativne aktivnosti sistema likopen - γ-ciklodekstrin

| Solvent type | DMSO | | | | Distilled water | | | |
|---|---|---|---|---|---|---|---|---|
| Test concentration in the sample [mg/ml] | 0.250 | 0.500 | 1.00 | 2.00 | 0.250 | 0.500 | 1.00 | 2.00 |
| **DPPH radical scavenging activity [%]** | 3.42 | 3.57 | 5.80 | 13.4 | 1.15 | 4.31 | 9.92 | 21.4 |
| | 6.24 | 4.61 | 6.54 | 11.7 | 4.74 | 5.32 | 9.29 | 20.4 |
| | 3.87 | 5.35 | 7.28 | 11.4 | 5.75 | 6.04 | 15.5 | 23.4 |
| | 2.68 | 8.03 | 6.54 | 12.8 | 5.46 | 6.90 | 9.78 | 16.7 |
| | 1.19 | 5.35 | 6.39 | 12.0 | 5.75 | 8.34 | 9.78 | 14.8 |
| | 3.87 | 2.83 | 6.24 | 11.9 | 5.55 | 9.07 | 10.9 | 14.3 |
| | 3.42 | 2.97 | 6.54 | 11.4 | 5.54 | 5.03 | 10.9 | 12.6 |
| | 4.46 | 2.08 | 5.50 | 12.3 | 5.53 | 7.00 | 11.0 | 20.9 |
| Average activity value | 3.64 | 4.35 | 6.36 | 12.1 | 4.93 | 6.50 | 10.9 | 18.1 |
| Standard deviation | 1.44 | 1.91 | 0.5374 | 0.674 | 1.56 | 1.64 | 1.98 | 3.98 |
| Coefficient of variation | 0.396 | 0.440 | 0.0845 | 0.0555 | 0.316 | 0.253 | 0.182 | 0.220 |
| **$EC_{50}$ [mg/ml]** | **9.71** | | | | **6.20** | | | |

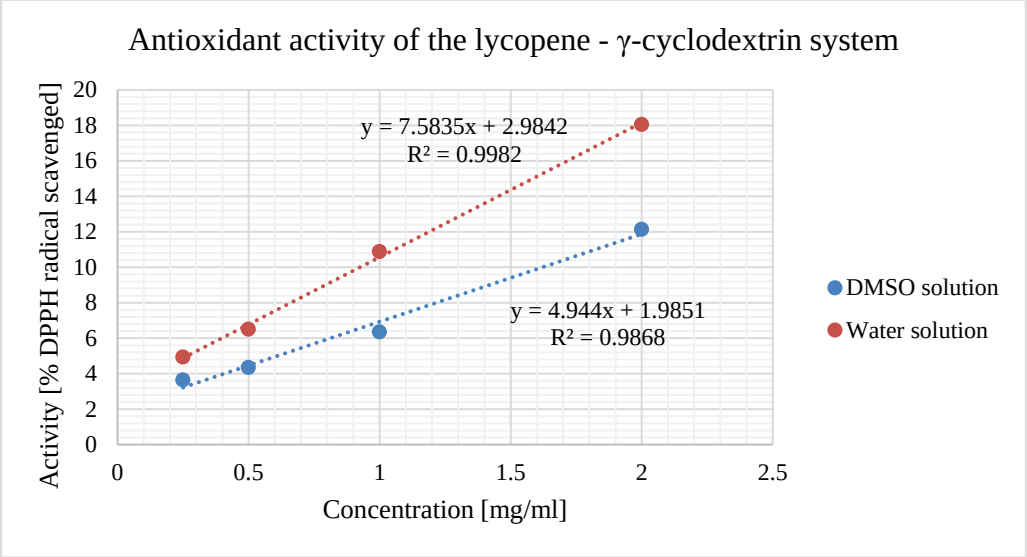


**Figure 16. Chart of the antioxidant activity of the lycopene - γ-cyclodextrin system**
**Slika 16. Grafički prikaz antioksidativne aktivnosti sistema likopen - γ-ciklodekstrin**

**Table VI** Results of studies on the antioxidant activity of the lycopene-β-cyclodextrin system

**Tabela VI** Rezultati istraživanja antioksidativne aktivnosti likopen-β-ciklodekstrinskog sistema

| Solvent type | DMSO | | | | Distilled water | | | |
|---|---|---|---|---|---|---|---|---|
| Test concentration in the sample [mg/ml] | 0.250 | 0.500 | 1.00 | 2.00 | 0.250 | 0.500 | 1.00 | 2.00 |
| **DPPH radical scavenging activity [%]** | 5.63 | 15.7 | 14.5 | 29.0 | 1.20 | 8.95 | 6.71 | 20.8 |
| | 3.12 | 9.81 | 15.5 | 19.3 | 1.55 | 4.64 | 9.46 | 12.9 |
| | 3.96 | 9.98 | 14.7 | 21.3 | 2.75 | 5.85 | 5.51 | 12.6 |
| | 6.1 | 8.97 | 15.3 | 21.3 | 0.688 | 2.24 | 8.95 | 14.1 |
| | 4.80 | 8.31 | 14.3 | 22.0 | 1.20 | 3.78 | 9.12 | 15.5 |
| | 5.96 | 8.81 | 14.8 | 20.8 | 1.22 | 4.27 | 7.24 | 12.3 |
| Average activity value | 4.93 | 10.3 | 14.9 | 22.3 | 1.44 | 4.96 | 7.83 | 14.7 |
| Standard deviation | 1.20 | 2.72 | 0.466 | 3.41 | 0.701 | 2.28 | 1.59 | 3.21 |
| Coefficient of variation | 0.244 | 0.265 | 0.0314 | 0.153 | 0.488 | 0.461 | 0.203 | 0.219 |
| **$EC_{50}$ [mg/ml]** | **4.89** | | | | **6.87** | | | |

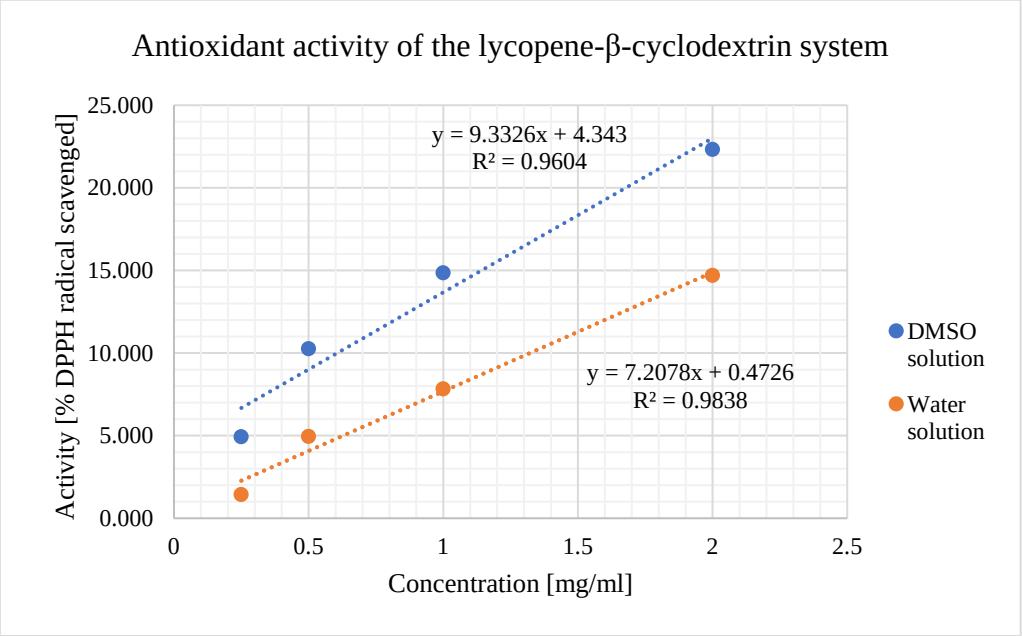


**Figure 17. Chart of the antioxidant activity of the lycopene - β-cyclodextrin system**

**Slika 17. Grafički prikaz antioksidativne aktivnosti sistema likopen - β-ciklodekstrin**

**Table VII** Results of studies on the antioxidant activity of the lycopene -2-hydroxypropyl-β-cyclodextrin system

**Tabela VII** Rezultati istraživanja antioksidativne aktivnosti likopen-2-hidroksipropil-β-ciklodekstrinskog sistema

| Solvent type | DMSO | | | | Distilled water | | | |
|---|---|---|---|---|---|---|---|---|
| Test concentration in the sample [mg/ml] | 0.250 | 0.500 | 1.00 | 2.00 | 0.250 | 0.500 | 1.00 | 2.00 |
| **DPPH radical scavenging activity [%]** | 4.63 | 12.5 | 15.0 | 28.4 | 3.96 | 8.95 | 11.0 | 18.6 |
| | 6.97 | 7.64 | 14.0 | 19.5 | 1.55 | 3.96 | 11.5 | 17.9 |
| | 7.64 | 9.98 | 13.8 | 21.0 | 3.27 | 4.99 | 11.5 | 16.5 |
| | 7.64 | 10.1 | 15.2 | 21.9 | 4.47 | 3.27 | 10.8 | 18.1 |
| | 6.47 | 11.0 | 14.7 | 20.7 | 4.64 | 4.64 | 11.7 | 17.4 |
| Average activity value | 6.67 | 10.2 | 14.5 | 22.3 | 3.58 | 5.16 | 11.3 | 17.7 |
| Standard deviation | 1.24 | 1.76 | 0.596 | 3.50 | 1.25 | 2.22 | 0.373 | 0.783 |
| Coefficient of variation | 0.186 | 0.172 | 0.0410 | 0.157 | 0.351 | 0.430 | 0.0330 | 0.0443 |
| **$EC_{50}$ [mg/ml]** | **5.17** | | | | **5.87** | | | |

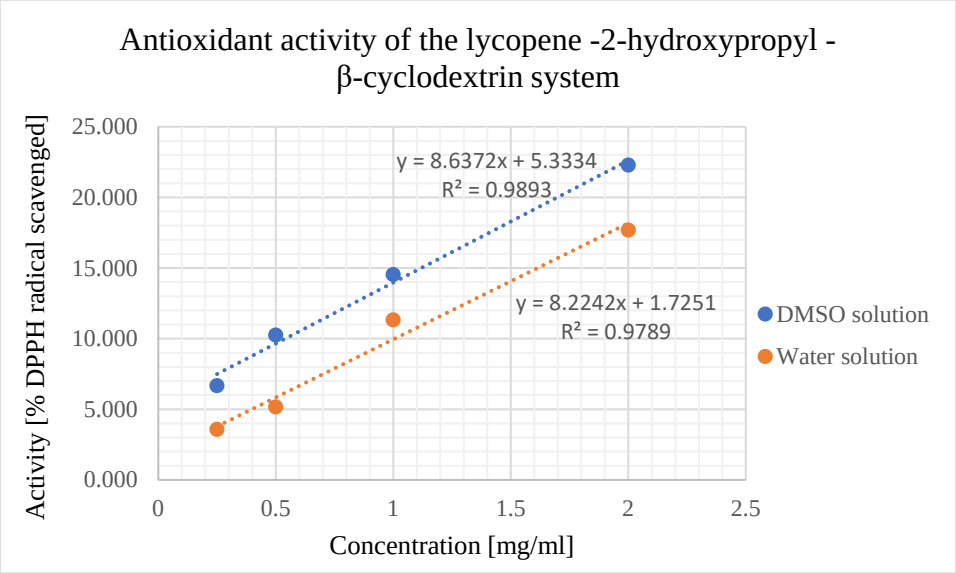


**Figure 18. Chart of the antioxidant activity of the lycopene - 2-hydroxypropyl-β-cyclodextrin system**

**Slika 18. Grafički prikaz antioksidativne aktivnosti sistema likopen - 2-hidroksipropil-β-ciklodekstrin**

To determine the antioxidant activity of the resulting extracts and cyclodextrin systems, a method using the free DPPH radical was used. Ascorbic acid was used as a standard substance. The $EC_{50}$ parameter was used to analyse and compare the results obtained. It expresses the concentration of an antioxidant that inhibits half of the free radicals. The lower the $EC_{50}$ value, the greater the antioxidant potential of the test compound. The results obtained are summarised in a chart (Figure 19).

The $EC_{50}$ value of the extracts and cyclodextrin systems was compared to the antioxidant power of ascorbic acid. Acetone extract has 0.112% of the antioxidant power of ascorbic acid, supercritical extract 0.0798%, lycopene - γ-cyclodextrin system 0.127% in water, 0.081% in DMSO, lycopene - β-cyclodextrin system 0.115% in water, 0.161% in DMSO, lycopene - 2-hydroxypropyl-β-cyclodextrin system 0.134% in water, 0.152% in DMSO.

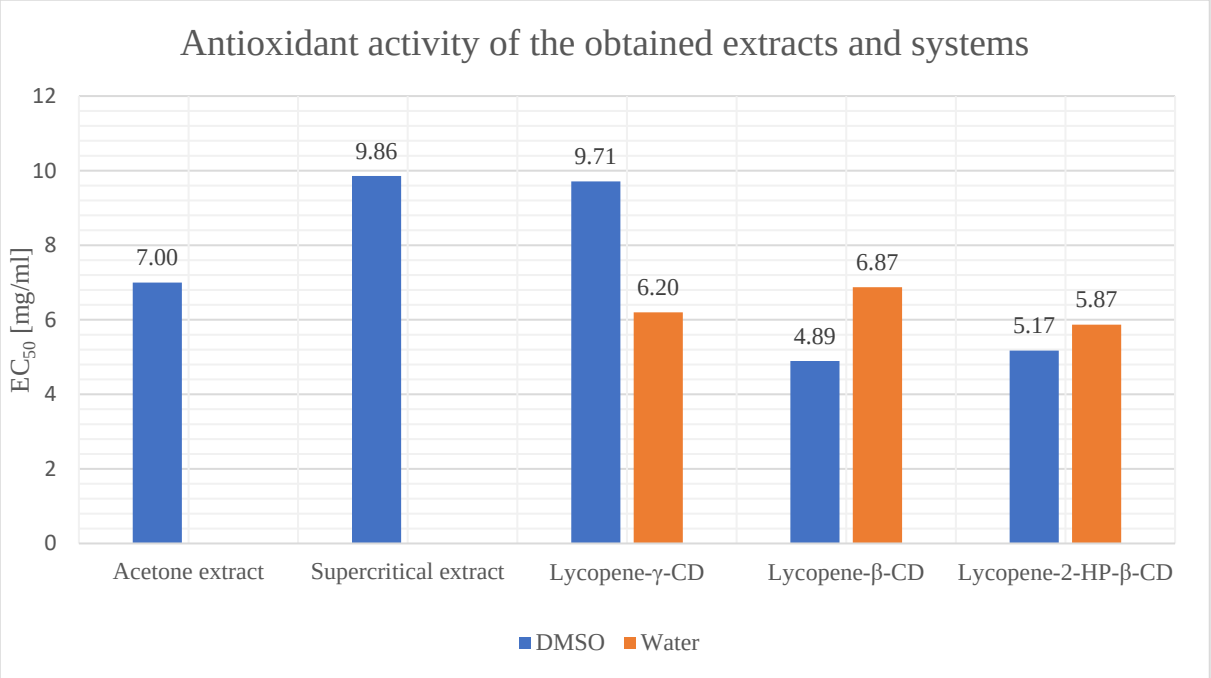


**Figure 19. Comparison of the antioxidant activity of the obtained extracts and lycopene-cyclodextrin systems**

**Slika 19. Poređenje antioksidativne aktivnosti dobijenih ekstrakata i sistema likopen-ciklodekstrin**

## Discussion

Wavelength shifts of the bands characteristic of cyclodextrins are considered to be the primary observation in FT-IR analysis of the extract-cyclodextrin system. These shifts occur due to the resulting intermolecular interactions caused by the incorporation of the extract into the γ-CD cavity. In the spectrum, cyclodextrin-related bands such as those corresponding to hydroxyl (OH) groups are a kind of a marker indicating the formation of interactions.

In the case of extract-cyclodextrin systems, numerous shifts of cyclodextrin-specific bands can be observed on the spectra, indicating the formation of intermolecular interactions.

In the case of the extract + β-CD and extract + 2-HP-β-CD systems, an extract-derived band (453 $cm^{-1}$) is observed, visible at 461 $cm^{-1}$. The presence of this peak may suggest that full inclusion may not occur for these systems.

The observed shifts could be attributed to hydrogen bond formation or other non-covalent interactions between the extract and cyclodextrin. These interactions alter the electron density and vibrational modes in the cyclodextrin molecule, causing changes in the absorption spectrum. The incorporation of the extract into the cyclodextrin cavity modifies the molecular environment and leads to observable changes in the FT-IR

spectrum. By comparing the shifted bands with the reference spectra of cyclodextrin, it was possible to confirm the formation of interactions between the individual components of the systems (which was also confirmed by XRD analysis).

Similar results were obtained by Jhan et al. (22), who investigated the formation of an inclusion complex between lycopene and β-CD using FT-IR. The numerous band shifts observed confirmed the formation of the inclusion complex.

In another study, Ma et al. (23) also observed band shifts in the FT-IR analysis. These indicated the formation of hydrogen bonds between lycopene and hydroxypropyl-beta-cyclodextrin.

In our study, no sharp and intense reflections (Bragg peaks) were observed in the diffractogram of pure tomato powder (Figure 4), confirming its crystalline nature. The extraction process with supercritical $CO_2$ resulted in the appearance of only one peak maximum instead of two, which may suggest changes in the structure of the tomato powder sample. Nevertheless, the sample still remains amorphous.

By comparing the experimental diffractograms of the extract, β-CD, physical mixture and system (Figure 5), it can be concluded that an inclusion complex was obtained by the run-off method. The peak shift and the altered shape of the diffractogram suggest the formation of strong interactions between the components of the systems.

Similar results were obtained by Jia and co-workers for berberine systems with β-CD (24). In their work, they confirmed the crystalline structure of cyclodextrin and berberine, the presence of crystalline peaks of both components in the physical mixture and the full disappearance of these characteristic reflections for the inclusion complex. The authors highlighted that the disappearance of the Bragg peaks for β-CD and berberine confirms the obtaining of the inclusion complex and the formation of the amorphous form of β-CD.

In contrast to β-CD, pure HP-β-CD occurs in an amorphous form (Figure 6, red line), as confirmed by numerous literature reports (25–27).

Due to the amorphous form of 2-HP-β-cyclodextrin and the lack of significant differences between the diffractogram of the system and the diffractogram of the physical mixture (Figure 6), it is not possible to determine unequivocally whether an inclusion complex has formed between the components of the system.

The change in the intensity of the reflections corresponding to pure γ-CD in the diffractogram of the extract-γ-CD system (Figure 7) may indicate the formation of an interaction between the components.

However, in contrast to the system obtained with β-CD, we do not observe a full 200morphization of cyclodextrin in this case.

The results of our study showed that the extracted lycopene practically is not dissolved in the acidic environment (1%). Only when it was combined with cyclodextrins was an improved *in vitro* dissolution in 0,1 M HCl observed.

Similar results were obtained by Binsuwaidan et al. (28), who compared the *in vitro* dissolution of pure lycopene and lycopene released from colloidal carriers, i.e. bilosomes, which are lipid-based vesicles that additionally contained bile acid salts. The dissolution of pure lycopene was 19.7%, while the use of colloidal carriers increased the dissolution of lycopene to 27.6%.

In our study, the antioxidant activity of the tested extracts was 6.9984 mg/ml and 9.8578 mg/ml for the acetone and supercritical extract, respectively. In both cases, the solvent was a DMSO solution due to the poor solubility of the extracts in water. These are significantly higher values in comparison with the standard ascorbic acid, whose $EC_{50}$ is 0.0079 mg/ml. A similar relationship was observed in a study by Firdrianny et al. (29).

The results of our study for the systems obtained indicate that combinations of lycopene with cyclodextrins increased the solubility of the supercritical extract in water and improved the antioxidant properties of the compound.

Other researchers have also observed the effect of the combination of lycopene with cyclodextrin on its antioxidant properties. Wang et al. (2) compared the activity of lycopene and inclusion complexes of lycopene with β-CD produced by co-precipitation. DPPH scavenging activity was higher for lycopene-β-CD complexes than for lycopene. However, the study also showed that there was no significant difference in the scavenging activity of superoxide anions and free radicals for lycopene and its β-CD inclusion complexes over the concentration range tested (2).

## Conclusions

Extraction with supercritical $CO_2$ yields lycopene-containing preparations. XRD analysis confirmed the amorphous nature of the supercritical extract and the formation of an inclusion complex between the components of the extract-β-cyclodextrin system. The study confirmed that the systems of lycopene with cyclodextrins increase its solubility in polar solvents. Neither acetone nor the supercritical extract are dissolved in 0.1 M HCl. The combinations of lycopene with cyclodextrins significantly increase its dissolution in an acidic environment. Of the excipients used in this study, 2-hydroxypropyl-β-cyclodextrin is the best excipient for formulating lycopene dissolution in the stomach. DPPH radical antioxidant activity studies showed that the acetone extract showed better antioxidant activity compared to the supercritical extract. Lycopene-cyclodextrin combinations significantly increase its antioxidant activity.

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## Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## CRediT authorship contribution statement

**Anna Kulawik:** Investigation, Formal analysis, Funding acquisition, Software, Methodology, Validation, Writing – original draft. **Natalia Rosiak:** Investigation, Methodology, Writing – original draft. **Andrzej Miklaszewski:** Investigation, Methodology. **Judyta Cielecka-Piontek:** Writing – original draft. **Przemysław Zalewski**: Conceptualization, Supervision, Writing – review & editing.

## References


1. Imran M, Ghorat F, Ul-Haq I, Ur-Rehman H, Aslam F, Heydari M, et al. Lycopene as a Natural Antioxidant Used to Prevent Human Health Disorders. Antioxidants. 2020 Aug 4;9(8):706.
2. Wang H, Wang S, Zhu H, Wang S, Xing J. Inclusion Complexes of Lycopene and β-Cyclodextrin: Preparation, Characterization, Stability and Antioxidant Activity. Antioxidants. 2019 Aug 16;8(8):314.
3. Kulawik A, Cielecka-Piontek J, Zalewski P. The Importance of Antioxidant Activity for the Health-Promoting Effect of Lycopene. Nutrients. 2023 Jan;15(17):3821.
4. Park H, Kim YJ, Shin Y. Estimation of daily intake of lycopene, antioxidant contents and activities from tomatoes, watermelons, and their processed products in Korea. Appl Biol Chem. 2020 Dec;63(1):50.
5. Carvalho GC, de Camargo BAF, de Araújo JTC, Chorilli M. Lycopene: From tomato to its nutraceutical use and its association with nanotechnology. Trends Food Sci Technol. 2021 Dec 1;118:447–58.
6. Caseiro M, Ascenso A, Costa A, Creagh-Flynn J, Johnson M, Simões S. Lycopene in human health. LWT. 2020 Jun;127:109323.
7. Khan UM, Sevindik M, Zarrabi A, Nami M, Ozdemir B, Kaplan DN, et al. Lycopene: Food Sources, Biological Activities, and Human Health Benefits. Oxid Med Cell Longev. 2021 Nov 19;2021:1–10.
8. Sun X, Jia H, Xu Q, Zhao C, Xu C. Lycopene alleviates H 2 O 2 -induced oxidative stress, inflammation and apoptosis in bovine mammary epithelial cells via the NFE2L2 signaling pathway. Food Funct. 2019;10(10):6276–85.
9. Li N, Wu X, Zhuang W, Xia L, Chen Y, Wu C, et al. Tomato and lycopene and multiple health outcomes: Umbrella review. Food Chem. 2021 May;343:128396.
10. Chen J, Cao X, Huang Z, Chen X, Zou T, You J. Research Progress on Lycopene in Swine and Poultry Nutrition: An Update. Animals. 2023 Feb 28;13(5):883.
11. Grabowska M, Wawrzyniak D, Rolle K, Chomczyński P, Oziewicz S, Jurga S, et al. Let food be your medicine: nutraceutical properties of lycopene. Food Funct. 2019;10(6):3090–102.
12. Amorim A das GN, Vasconcelos AG, Souza J, Oliveira A, Gullón B, de Souza de Almeida Leite JR, et al. Bio-Availability, Anticancer Potential, and Chemical Data of Lycopene: An Overview and Technological Prospecting. Antioxidants. 2022 Feb 11;11(2):360.

13. Mehta N, Patani P, Singhvi I. A review on tomato lycopene. Int J Pharm Sci Res. 2018;9(3):916-23.
14. Bin-Jumah MN, Nadeem MS, Gilani SJ, Mubeen B, Ullah I, Alzarea SI, et al. Lycopene: A Natural Arsenal in the War against Oxidative Stress and Cardiovascular Diseases. Antioxidants. 2022 Jan 26;11(2):232.
15. Carvalho GC, Sábio RM, Chorilli M. An Overview of Properties and Analytical Methods for Lycopene in Organic Nanocarriers. Crit Rev Anal Chem. 2020 May 15;1–13.
16. Leh HE, Lee LK. Lycopene: A Potent Antioxidant for the Amelioration of Type II Diabetes Mellitus. Molecules. 2022 Apr 4;27(7):2335.
17. Wu H, Wu Y, Cui Z, Hu L. Nutraceutical delivery systems to improve the bioaccessibility and bioavailability of lycopene: A review. Crit Rev Food Sci Nutr. 2023 Jan 19;1–19. doi: 10.1080/10408398.2023.2168249. Epub ahead of print.
18. Murakami K, Goto M, Honda M. High-temperature Supercritical CO2 Extraction of Lycopene from Tomato Powder for Enhancing Z-Isomerization and Recovery of Lycopene. J Oleo Sci. 2022;71(9):1289–97.
19. Banchero M. Supercritical Carbon Dioxide as a Green Alternative to Achieve Drug Complexation with Cyclodextrins. Pharmaceuticals. 2021 Jun 11;14(6):562.
20. Stasiłowicz-Krzemień A, Cielecka-Piontek J. Hop Flower Supercritical Carbon Dioxide Extracts Coupled with Carriers with Solubilizing Properties—Antioxidant Activity and Neuroprotective Potential. Antioxidants. 2023 Sep 5;12(9):1722.
21. Barba AIO, Hurtado MC, Mata MCS, Ruiz VF, Tejada MLSD. Application of a UV–vis detection-HPLC method for a rapid determination of lycopene and β-carotene in vegetables. Food Chem. 2006 Mar;95(2):328–36.
22. Jhan S, Pethe AM. Double-loaded liposomes encapsulating lycopene β-cyclodextrin complexes: preparation, optimization, and evaluation. J Liposome Res. 2020 Jan 2;30(1):80–92.
23. Ma Y, Zhong L, Peng Z, Liu X, Ouyang D, Guan S. Development of a Highly Water-Soluble Lycopene Cyclodextrin Ternary Formulation by the Integrated Experimental and Modeling Techniques. AAPS PharmSciTech. 2021 Jan;22(1):5.
24. Jia J, Zhang K, Zhou X, Zhou D, Ge F. Precise Dissolution Control and Bioavailability Evaluation for Insoluble Drug Berberine via a Polymeric Particle Prepared Using Supercritical CO2. Polymers. 2018 Oct 26;10(11):1198.
25. Stasiłowicz A, Tykarska E, Lewandowska K, Kozak M, Miklaszewski A, Kobus-Cisowska J, et al. Hydroxypropyl-β-cyclodextrin as an effective carrier of curcumin – piperine nutraceutical system with improved enzyme inhibition properties. J Enzyme Inhib Med Chem. 2020 Jan 1;35(1):1811–21.
26. Stasiłowicz-Krzemień A, Rosiak N, Płazińska A, Płaziński W, Miklaszewski A, Tykarska E, et al. Cyclodextrin Derivatives as Promising Solubilizers to Enhance the Biological Activity of Rosmarinic Acid. Pharmaceutics. 2022 Sep 30;14(10):2098.
27. Li J, Zhang S, Zhou Y, Guan S, Zhang L. Inclusion complexes of fluconazole with β-cyclodextrin and 2-hydroxypropyl-β-cyclodextrin in aqueous solution: preparation, characterization and a structural insight. J Incl Phenom Macrocycl Chem. 2016 Apr;84(3–4):209–17.

28. Binsuwaidan R, Sultan AA, Negm WA, Attallah NGM, Alqahtani MJ, Hussein IA, et al. Bilosomes as Nanoplatform for Oral Delivery and Modulated In Vivo Antimicrobial Activity of Lycopene. Pharmaceuticals. 2022 Aug 24;15(9):1043.
29. Fidrianny I, Rizkiya A, Ruslan K. Antioxidant activities of various fruit extracts from three solanum sp. using DPPH and ABTS method and correlation with phenolic, flavonoid and carotenoid content. J Chem Pharm Res. 2015;7(5):666–72.

# Ispitivanje ciklodekstrina kao potencijalnih nosača likopena

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## Kratak sadržaj

Likopen je karotenoid sa visokom antioksidativnom aktivnošću. Brojne studije pokazuju njegove pozitivne efekte u prevenciji i ublažavanju mnogih bolesti. Međutim, zbog slabe rastvorljivosti u vodi, njegova upotreba je veoma ograničena. Razvijanje formulacije sa likopenom sa povoljnim terapijskim efektima omogućiće njegovu efikasniju upotrebu. Cilj ovog rada je stoga bio da se superkritičnom ekstrakcijom dobiju preparati koji sadrže likopen, kao i dobijanje kompleksa likopena iz ekstrakta sa ciklodekstrinima radi poboljšanja njegove rastvorljivosti i povećanja njegovog antioksidativnog potencijala. Ekstrakti koji sadrže likopen dobijeni su ultrazvučnom ekstrakcijom acetona i ekstrakcijom u superkritičnoj fazi. Superkritični ekstrakt je kombinovan sa γ-ciklodekstrinom, β-ciklodekstrinom i 2-hidroksipropil-β-ciklodekstrinom. Za dobijene sisteme i ekstrakte urađene su Infracrvena spektroskopija sa *Fourierov*-om transformacijom oslabljene ukupne refleksije (ATR-FTIR) i Rendgenska difrakcija (XRD). Aparat sa lopaticama je korišćen za procenu *in vitro* rastvaranja, a sakupljeni uzorci su analizirani pomoću HPLC. Antioksidativna aktivnost je procenjena primenom 2,2-difenilo-1-pikrilohidrazil (DPPH) metode. Rezultati pokazuju da ciklodekstrini povećavaju rastvaranje likopena u kiseloj sredini i povećavaju antioksidativni potencijal jedinjenja. Zaključujemo da će razvoj formulacije koja sadrži kombinaciju likopena dobijenog superkritičnom ekstrakcijom i ciklodekstrina omogućiti širu i efikasniju upotrebu ovog sastojka.

**Ključne reči:** likopen, ekstrakcija superkritičnom tečnošću, ciklodekstrini, sistem za dostavu leka, antioksidans