

Physical and Chemical Properties of *Crataegus monogyna* Jacq. var. *monogyna* Fruits Growing in Isparta/Turkiye

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Abstract

Aim of study: This study investigated the physical and chemical properties of *Crataegus monogyna* Jacq. fruits.

Area of study: The study area is around Gölcük Lake in Isparta province located in the Mediterranean region.

Material and method: Morphological traits, such as fruit features, and color metrics (L^* , a^* , b^*), of *Crataegus monogyna* Jacq. var. *monogyna* were analyzed over three-month periods, revealing seasonal variations influenced by ripening stages and environmental conditions.

Main results: The fruit width values in July, August and September were 7.62 mm, 8.28 mm, and 8.50 mm; the fruit length values were 9.47, 9.35, and 8.89 mm; and the fruit weight values were 0.39, 0.44, and 0.40 g, respectively. The L values were 24.3, 32.2, and 15.7; the a values were -29.3, 36.3, and 44.1; and the b values were 46.66, 40.06, and 29.70, respectively. Volatile compounds were profiled via GC-MS. The functional groups in the fruit extracts were determined through FT-IR spectroscopy.

Research highlights: The results emphasize the importance of harvest timing for optimal fruit quality and highlight the potential of hawthorn fruits for applications in food, pharmaceuticals, and cosmetics because of their bioactive and volatile components. These findings contribute to the understanding of the chemical and ethnobotanical value of *C. monogyna* and support its utilization in diverse sectors.

Keywords: *Crataegus monogyna* Fruit, Color, Volatile Components

Isparta/Turkiye'de Yetişen *Crataegus monogyna* Jacq. var. *monogyna* Meyvelerinin Fiziksel ve Kimyasal Özellikleri

Öz

Çalışmanın amacı: Bu çalışmada *Crataegus monogyna* Jacq. meyvelerinin fiziksel ve kimyasal özellikleri incelenmiştir.

Çalışma alanı: Çalışma alanı Akdeniz Bölgesi'nde yer alan Isparta ilinin Gölcük Gölü çevresidir.

Materyal ve yöntem: *Crataegus monogyna* Jacq. var. *monogyna*'ya ait meyve özellikleri ve renk ölçütleri (L^* , a^* , b^*) gibi morfolojik özellikler üç aylık dönemler boyunca analiz edilerek olgunlaşma aşamaları ve çevresel koşullardan etkilenen mevsimsel varyasyonlar ortaya çıkarılmıştır.

Temel sonuçlar: Temmuz, Ağustos ve Eylül aylarında meyve çapı değerleri sırasıyla 7.62, 8.28 ve 8.50 mm; meyve boyu değerleri 9.47, 9.35 ve 8.89 mm; meyve ağırlığı değerleri ise 0.39, 0.44 ve 0.40 g olarak belirlenmiştir. L değerleri sırasıyla 24.3, 32.2 ve 15.7; a değerleri -29.3, 36.3 ve 44.1; b değerleri ise 46.66, 40.06 ve 29.70'tir. Uçucu bileşiklerin profili GC-MS aracılığıyla çıkarılmıştır. Meyve özütlerindeki fonksiyonel gruplar FT-IR spektroskopisi ile belirlenmiştir.

Araştırma vurguları: Sonuçlar, optimum meyve kalitesi için hasat zamanlamasının önemini vurgulamakta ve ilaç meyvelerinin biyoaktif ve uçucu bileşenleri nedeniyle gıda, ilaç ve kozmetik alanlarındaki uygulamalarda kullanım potansiyelini ortaya koymaktadır. Bu bulgular, *C. monogyna*'nın kimyasal ve etnobotanik değerinin anlaşılmasına katkıda bulunmakta ve farklı sektörlerde kullanımını desteklemektedir.

Anahtar Kelimeler: *Crataegus monogyna* Meyvesi, Renk, Uçucu Bileşenler



Introduction

Today, applications such as hormones and pesticides applied to plants to meet the food needs of the increasing population have caused the food to move away from organicity, and it is thought that it has started to cause harm as well as benefit for humans. For this reason, in recent years, people have started to turn to more natural, drug-free plants. They have started to turn back to ancient plants whose usage patterns have been passed down from the past to the present through their elders and to plants whose benefits have been proven by scientific research.

Traditional herbs and natural plants contain many bioactive compounds that can be used as food and medicine (Zhang et al., 2022). Hawthorn, known as the “nutritious fruit”, belongs to the Rosaceae family and is usually found on forest edges and mountain slopes in lower and warmer areas (Lund et al., 2017; Lou et al., 2020; Brown, 1995; Grieve, 1982; Wichtl, 1996). Hawthorn is widespread worldwide and is known to include more than one thousand species (Ma and Lu, 2016). Mostly in the temperate regions of the Northern Hemisphere. *Crataegus monogyna* and *C. laevigata* are the main hawthorn species in Central Europe, whereas *C. pentagyna*, *C. nigra* and *C. azarolus* are the hawthorn species of Southern and Southeastern Europe (Du et al., 2019; Wang et al., 2013; Ozderin et al., 2016; Ozderin, 2024).

Color is a distinguishing feature in characters such as fruit and wood. By examining the color of the materials, some information about some properties can be obtained. To date, many researchers have investigated the color properties of the materials they have studied, such as L, a, b and deltaE (ΔE) (Serçe et al., 2011; Coklar et al., 2018; Dursun et al., 2021; Sahin et al., 2023; Kaytanlioglu et al., 2024; Özkan et al., 2025).

Hawthorn is mostly used in food and pharmaceutical research (Zhang et al., 2022). Fresh or dried fruits are used for many purposes. Red hawthorn fruits (*C. monogyna*) are recommended in folk medicine because they are healthy and nutritious and are used to treat colds, bronchitis, cellulite, obesity, menopause, hypertension, heart failure,

cholesterol lowering, digestive system disorders, cancer, hyperglycemia, and anxiety and can be jam, jelly, drink, and wine (Schüssler et al., 1995; Camejo-Rodrigues et al., 2003; Novais et al., 2004; ardo de Santayana et al., 2007; Bernatoniene et al., 2008; Tadić et al., 2008; Salehi et al., 2009; Wang, 2015; Venskutonis, 2018; Nazhand et al., 2020; Li et al., 2022). Plants that are used for food and medicine and are naturally distributed in the region need to be studied because they contain greater amounts of bioactive components than cultivated plants do (Heinrich, 2005).

The wild edible fruits ripen in August–September, and both flowers and fruits contain many bioactive compounds, such as flavonoids, tannins and pectins (Landzhev, 2005). Owing to the presence of these compounds, many studies have been conducted using extracts of this plant in the production of distilled spirits (Kostik et al., 2014). In some studies, compounds such as esters, high alcohols, aldehydes, and terpenes have been shown to provide flavor in beverages (Marku et al., 2015; Yankov et al., 2000). In wine production studies conducted with different fruits, hawthorn flowers and fruits were added as flavors for wine distillates because of their volatile components (Marinov, 2005; Tesevic et al., 2009; Lukic et al., 2011; Kostik et al., 2014). In a study in which vinegar and wine were made from hawthorn fruits, organic acids and some bioactive compounds were detected (Özdemir et al., 2022). In addition to compounds such as gallic acid and caffeic acid, acetic acid, phenylacetic acid, and acetoin, followed by pentanoic acid, benzoic acid, (E)-isoleucenol, 2-cyclohexenone, propanoic acid, cavidol and diethyl succinate, which are thought to have positive effects on human health, have been proven to be present in vinegar made from hawthorn fruits. It has also been suggested that hawthorn and hawthorn vinegar have antioxidant, antimicrobial and anti-inflammatory properties and that fruit pulp can be used in other sectors, such as cosmetics (Güven et al., 2006; Ebrahimzadeh & Bahramian, 2009; Bahorun et al., 2003; Kirakosyan et al., 2003). In addition, the organic components observed in the FT-IR spectrum have been studied by

many researchers, and the wavelengths at which the organic components in the spectrum are located have been revealed (Yilgor et al., 2013; Ceylan & Pekgözlü, 2019; Bayram et al., 2024).

Owing to the abovementioned properties of hawthorn fruit, this study was carried out to determine the physical and chemical properties of the red hawthorn (*Crataegus monogyna* var. *monogyna*) species distributed in the Gölcük region in Isparta and to obtain information about its ethnobotanical and medicinal value from its volatile components and its landscape value from its fruit morphological characteristics.

Material and Methods

Study Area

Fresh wild hawthorn fruits were collected from hawthorn trees growing from Gölcük (Isparta) in Turkey in July, August and September 2024 (Figure 1, Figure 2). The fruits were subsequently transported in polypropylene bags and held at room temperature. Width, length, weight, color and

sugar values were immediately measured upon arrival.

Morphological Traits

To determine the weight of the fruits, three groups of samples consisting of 100 fruits were selected randomly and measured with a digital scale (± 0.01 g). Thirty fruits were taken from each group, and their width and length were measured with a digital caliper (± 0.01 mm).

Color Measurements

To determine color values, three groups of samples consisting of thirty fruits were selected randomly. The CIE $L^*a^*b^*$ 1976 (Commission Internationale d'Eclairage) standard was used to calculate the brightness/darkness (L^*), redness/greenness (a^*), yellowness/blueness (b^*) and total color differences (ΔE_{ab}) of the water samples automatically via Equations (1), (2), (3), and (4) below (Hach-Lange, 2023).

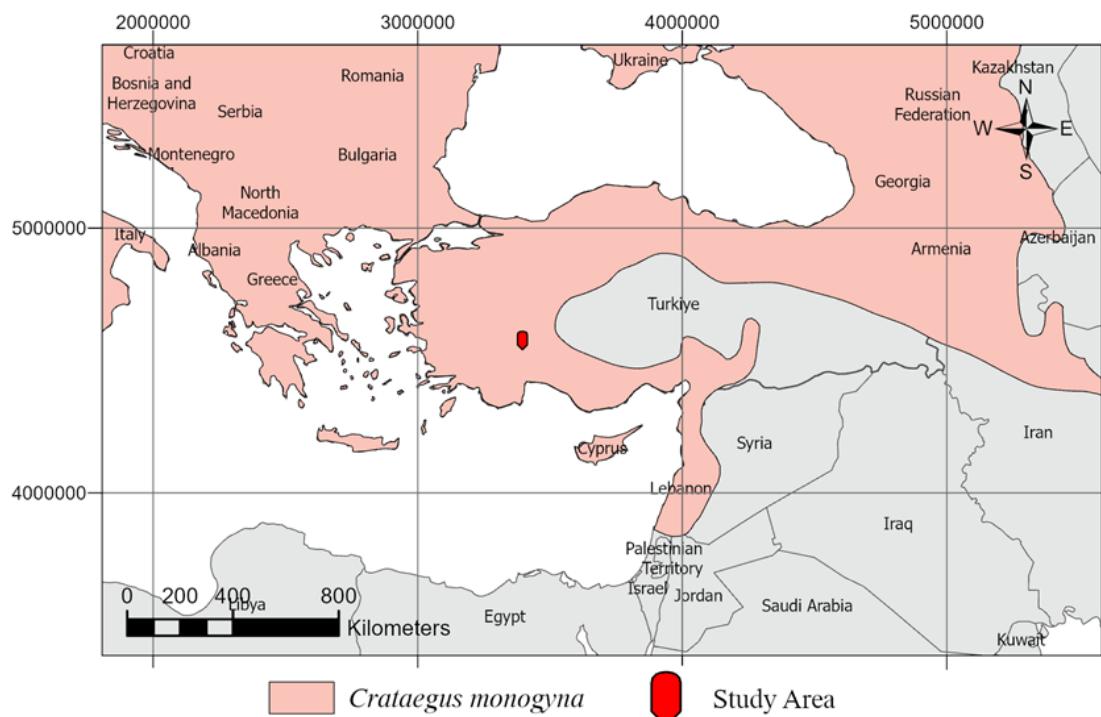


Figure 1. Map of the study area



Figure 2. Hawthorn fruits (1: July, 2: August, 3: September)

$$L: f(Y/Yn) - 16 \quad (1)$$

$$a: 500 [f(X/Xn) - f(Y/Yn)] \quad (2)$$

$$b: 200 [f(Y/Yn) - f(Z/Zn)] \quad (3)$$

$$\Delta E_{ab}: \sqrt{(\Delta L)^2 + (\Delta a)^2 + (\Delta b)^2} \quad (4)$$

In the equations, L represents the brightness/darkness level (a value between 0 and 100, and as the number decreases, the darkness increases, 0 represents black, 100 represents perfect whiteness), a represents redness/greenness, and b represents yellowness/blueness. ΔE describes the total color difference as a combination of all these. All of the calculations in the equations above were measured automatically with the help of an Nix2 handheld colorimeter (Nix Sensor Ltd., Hamilton, Canada).

Many researchers have reported that the total color difference (ΔE) of samples can be between 0 and 100, with smaller numbers explaining lower color differences and larger numbers explaining greater color differences (Janin et al., 2001; Sahin et al., 2011; Sahin & Onay, 2020). In general,

-If $\Delta E < 1.0$ (metric): color change cannot be distinguished by the human eye;

-If $1.0 < \Delta E < 3.0$ (metric): color change can be distinguished by the human eye when carefully examined;

-If $\Delta E > 3.0$ (metric), color change can be distinguished by the human eye when examined.

Brix Values of Fruits

The dissolved sugar and/or soluble solid content of a specific substrate are often measured using the degree Brix ($^{\circ}\text{Bx}$), which is a measurement of the dissolved solids in a liquid. Some researchers claim that the potential sugar content is proportional to the Brix value (Kappes et al., 2007; Chauhan et al., 2014). To estimate the fruit sugar content, a hand refractometer (Palm Abbe PA2021, Solon, OH) was used to measure the Brix value of 30 Hawthorn fruits from each group.

Volatile Component Analysis

The technique outlined by Sagdic et al. (2013) was used to separate the essential oil of hawthorn fruits via water distillation. A flask (1 L) containing approximately 100 g of fruit pulp was treated with distilled water (1:5 w:v) and hydrodistilled for one hour via Clevenger equipment (Ildam, Turkey; Tekeş et al., 2024). A cooling tunnel was used to extract the essential oils. Following anhydrous sodium sulfate drying and filtration to eliminate any remaining water, the essential oil was kept in sealed test tubes at -20°C until

needed. Using a Shimadzu QP 5050 GC-MS system with a quadrupole detector and an FFAP polar capillary column [50 m × 0.32 mm (i.d.), film thickness: 0.25], the volatile content of the hawthorn essential oil was ascertained.

The column temperature program was set to increase from 120 °C (1 min) to 230 °C at a rate of 6 °C per minute, and it was maintained at that temperature for 35 minutes. Each sample had a 1 µL injection volume, and the carrier gas was helium at 14 psi (split 1:10 mL/min). To identify volatile components, Flavor 2, NIST05, and Wiley7n libraries were used. By dividing the area of each peak by the area under the entire peak, peak areas were utilized to directly provide the essential oil's % volatile content.

FT-IR Measurements

FT-IR measurements were performed with the FT-IR-4700 type A device. The wavelength range was 400–4000 cm⁻¹ and the spectrum was taken at a resolution of 4 cm⁻¹.

Results and Discussion

Table 1 shows the means and standard deviations of the width, height and weight of the hawthorn fruits measured in July, August and September. The width values were the lowest in July (7.62 mm±0.42) and increased over time, reaching the highest level in August (8.28 mm±0.48) and September (8.50 mm±0.36), indicating a growth trend in width. The height, on the other hand, presented the highest mean value in July (9.47 g±0.62), with a slight decrease in August (9.35 g±0.68) and a further decrease in September, reaching the lowest level (8.89 g±0.40). In addition, the standard deviation was lower in September, indicating that the measurements became more stable. In terms of weight, hawthorn fruits reached the lowest value in July (0.39 g) and the highest value in August (0.44 g). In September, it decreased again slightly (0.40 g). In a study conducted in Isparta, it was concluded that the fruit weight of *C. monogyna* varied between 0.33 and 0.90 g (Nacakçı, 2022), and in studies conducted in Malatya, it was concluded that the fruit weights of individuals belonging to the *Crataegus* genus varied between 0.98 and 6.76 g (Bektaş et al., 2017) and between 0.76

and 4.27 g (Ercişli et al., 2015). Similar results were obtained in our present study.

Table 1. Average width (mm), height (mm) and weight (g) of hawthorn fruits

Months	Width	Height	Weight
July	7.62±0.42	9.47±0.62	0.39
August	8.28±0.48	9.35±0.68	0.44
September	8.50±0.36	8.89±0.40	0.40

Table 2 shows the changes in the means and standard deviations of the L (luminance), a (red–green axis) and b (yellow–blue axis) values of the hawthorn fruits measured during July, August and September. The L value was moderate in July (24.3±9.35), indicating high variability, and reached the highest value in August (32.2±4.87). The a value was dominated by green tones in July (-29.3±10.45), whereas in August and September, the value became positive, and red tones were dominant (36.3±5.70 and 44.1±7.28). When the b value was analyzed, yellow tones were dominant in July and August (46.66±7.81 and 40.06±7.28), whereas the b value decreased in September (29.70±9.10) and approached blue tones. The results indicate that the colors of hawthorn fruits become darker and closer to blue toward the end of summer, moving away from both light and yellow tones. These changes may be related to climatic conditions or seasonal effects. Coklar et al. (2018) reported an L value of 61.86, a value of 11.65 and b value of 49.07 in a study conducted with individuals from *C. orientalis*. Alirezalu et al. (2020) reported that the mean L*, a*, b* and brix values of *C. monogyna* samples were 7.37, 33.95, and 12.55, respectively, which is in line with our current results. Serçe et al. (2011) determined the L*, a*, and b* values of hawthorn samples to be 71.3%, 1.8%, and 49.4%, respectively, which is consistent with our current study.

Table 2. *Crataegus monogyna* var. *monogyna* fruit color characteristics

Months	L	a	b
July	24.3±9.35	-29.3±10.45	46.66±7.81
August	32.2±4.87	36.3±5.70	40.06±7.28
September	15.7±4.59	44.1±7.28	29.70±9.10

L: Luminance, a: Red–green axis, b: Yellow–blue axis

The delta E plot in Figure 3 represents a three-month period covering July, August and September and shows the metrics of color difference between the samples. Delta E is widely used in the literature to quantitatively express color differences. Figure 3 shows that there were significant fluctuations between fruit samples in July. Among the randomly measured fruits, high delta E values were obtained, whereas the July data showed sharp increases. Significant and irregular differences are likely to occur because of

climatic conditions or conditions related to the growing environment of the fruit. In contrast, the delta E values of the fruit samples collected in August presented a more moderate trend, with more consistent results than those collected in July. Finally, the fruits collected in September presented the lowest delta E values and the most stable results. These results indicate that fruits collected in September have regular color changes under more homogeneous conditions.

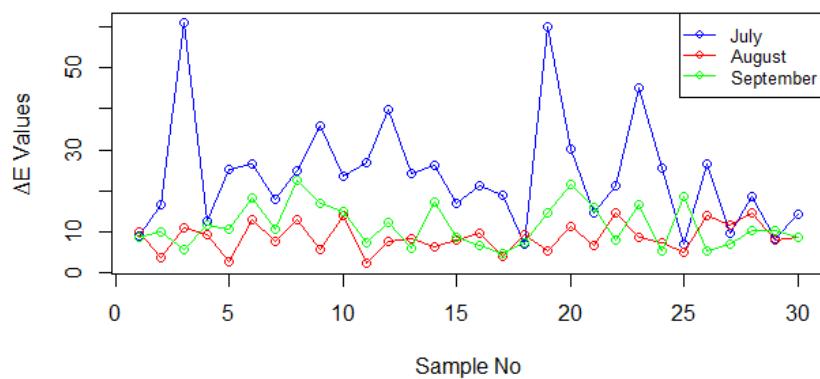


Figure 3. DeltaE (ΔE) values of hawthorn fruits

Figure 4 shows the Brix values of the hawthorn fruits measured in July, August and September. September had the highest Brix values among all sample numbers, indicating that sugar levels were highest in this month. The Brix values of the hawthorn fruits measured in August were generally higher than those measured in July but lower than those measured in September. In July, Hawthorn fruit presented the lowest Brix values among all the samples, indicating that it presented the lowest sugar levels. This increasing trend in Brix values suggests that sugar accumulation in fruits or plants increases over time, depending on the ripening process. Thus, a linear relationship can be demonstrated between the increase in sugar level and the ripening process. Moghadam & Kheiralipour (2015) reported brix values between 18.3 and 19 in *C. pontica* species. Similar results were obtained in our present study.

When the volatile components of the fruits were examined, 9 components were found to be common to all three groups. Hexanol, beta-Ocimene and 2-ethylfuran components were

detected only in July fruits; the α -pinene component was detected only in August fruits; and the (Z)-Hex-3-en-1-ol component was detected only in September fruits. (E)-4,8-Dimethyl-1,3,7-nonatriene was found in fruits in July and August. Ethanol, n-hexanol, eucalyptol (1,8-cineole) and nonanal components were found in August and September fruits.

When the retention times of the components common to the fruits of all three months were examined, it was determined that acetaldehyde, 2-propanone, hexanal, E)-hept-2-enal, (E)-2-hexenal and limonene components decreased from July to September; (E)-2-hexen-1-ol and beta-myrcene components were the lowest in August; and the cymol component was equal in July and August and decreased in September (Table 3).

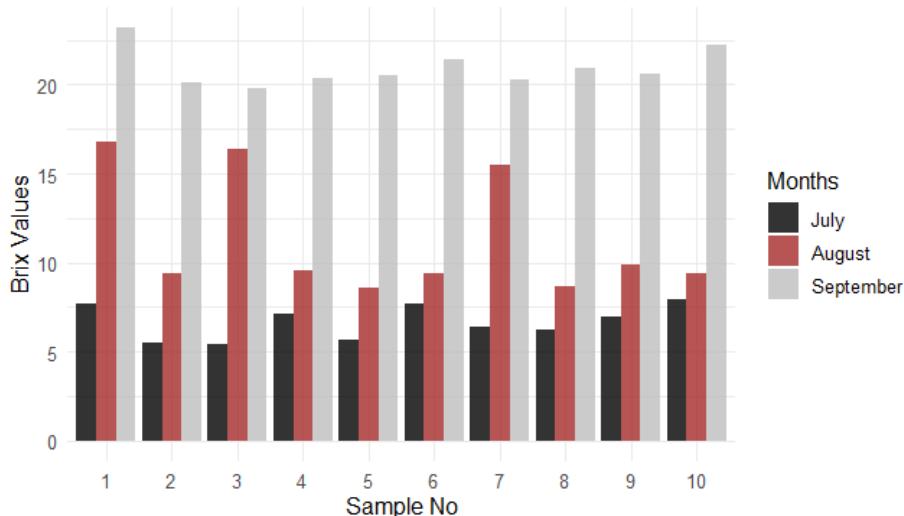


Figure 4. Brix values of hawthorn fruits

Table 3. Retention time (Rt) and Kováts retention indices (RI) of volatile components in July, August and September

Components	July		August		September	
	Rt	RI	Rt	RI	Rt	RI
Acetaldehyde	1.285	90	1.280	90	1.268	90
2-Propanone	1.428	304	1.422	304	1.407	304
Hexanal	4.551	671	4.549	671	4.538	671
(E)-Hept-2-enal	5.837	784	5.833	785	5.830	786
(E)-2-Hexenal	6.081	736	6.061	736	6.038	733
(E)-2-Hexen-1-ol	6.520	709	6.464	708	6.470	709
β- Myrcene	10.866	1077	10.841	1077	10.849	1077
Cymol	12.145	1087	12.145	1088	12.140	1088
Limonene	12.330	998	12.319	999	12.316	999

When the area and area% values of the volatile components were examined, the contents of the acetaldehyde and (E)-2-hexenal components decreased from July to September (Table 4). 2-Propanone, (E)-Hept-2-enal, beta-myrcene, thymol and limonene components were found to be highest in August fruits. The hexanal component was found to be lowest in August. The (E)-2-hexen-1-ol component increased from July to September.

The peak regions in the FTIR spectrum of organic components have been revealed by many researchers. In general, the peak wavelengths in the FTIR spectrum of organic components can be summarized as follows (Yilgor et al., 2013; Ceylan & Pekgözlü, 2019).

915-930 cm^{-1} : C-H bond in aromatic ring,
 1085-1030 cm^{-1} : C-O(H) and C-O(C) bonds,
 1370-1365 cm^{-1} : Vibration of phenolic OH groups,
 1430-1422 cm^{-1} : Aromatic C-C and C-H bonds,
 1515-1605 cm^{-1} : Aromatic C-C bonds,
 1675-1660 cm^{-1} and 1715-1710 cm^{-1} : C=O bonds
 2940-2820 cm^{-1} : C-H bonds (CH₃ and CH₂),
 3450-3400 cm^{-1} : Aliphatic and phenolic O-H bonds.

Table 4. Volatile compounds (area/area%) in July, August and September

(Area %)	July	August	September	(Area)	July	August	September
Acetaldehyde	0.31	0.27	0.26	Acetaldehyde	58655	51056	43738
2-Propanone	0.21	0.84	0.68	2-Propanone	40230	156012	116373
Hexanal	9.18	5.24	7.03	Hexanal	1731050	978409	1199424
(E)-Hept-2-enal	1.36	1.44	0.89	(E)-Hept-2-enal	257030	268221	151627
(E)-2-Hexenal	87.06	75.45	52.12	(E)-2-Hexenal	16423290	14080285	8893337
(E)-2-Hexen-1-ol	0.08	6.30	17.10	(E)-2-Hexen-1-ol	15409	1176404	2917077
Hexanol	0.10	-	-	Hexanol	19034	-	-
β- Myrcene	0.25	0.45	0.17	β- Myrcene	47394	84469	29160
Cymol	0.10	0.79	0.61	Cymol	19676	148104	103954
Limonene	0.42	1.68	1.15	Limonene	79343	313845	196322
β-Ocimene	0.45	-	-	β-Ocimene	84354	-	-
(E)-4,8-Dimethyl-1,3,7-nonatriene	0.27	0.30	-	(E)-4,8-Dimethyl-1,3,7-nonatriene	51109	56660	-
Ethanol	-	0.08	0.23	Ethanol	-	15386	39633
n-Hexanol	-	5.10	8.52	n-Hexanol	-	950985	1453183
alpha- Pinene	-	0.14	-	α- Pinene	-	27025	-
2-Ethylfuran	0.20	-	-	2-Ethylfuran	38302	-	-
(Z)-Hex-3-en-1-ol	-	-	8.71	(Z)-Hex-3-en-1-ol	-	-	1486101
Eucalyptol (1,8-Cineole)	-	1.55	1.97	Eucalyptol (1,8-Cineole)	-	289930	336539
Nonanal	-	0.35	0.57	Nonanal	-	65150	96779

Figure 5 shows the FT-IR graph of hawthorn fruit for the months of July, August and September. The graph shows distinct peaks and troughs at different wavelengths. This finding indicates that each month's sample shows differences in terms of characteristic chemical bonds or functional groups (Bayram et al., 2025). The hawthorn fruit in July presented the highest transmittance values in the 3000–400 cm^{-1} range, whereas the fruit sample in September generally presented the lowest transmittance levels. The August sample lies between these two months and shows a more balanced permeability profile. The different intensities of the absorption bands, especially those at approximately 3000 cm^{-1} and 1000 cm^{-1} ,

reflect changes in the chemical structure or variations in the molecular composition of the substances in each month. When these data are evaluated, it can be concluded that hawthorn fruits are exposed to various climatic conditions over time. When the FT-IR results of the *C. monogyna* fruit extract and the FT-IR data obtained after the reaction with the gold salt were examined, the frequency shifts of the functional groups involved in the reduction were 3347 cm^{-1} , 1634 cm^{-1} and 2110 cm^{-1} . The shifts in these frequencies suggest that -OH (hydroxyl) groups (Aktepe and Baran, 2021), N-H (amine) groups (Atalar et al., 2021) and C≡C (alkyne) groups are the functional groups involved in the reduction.

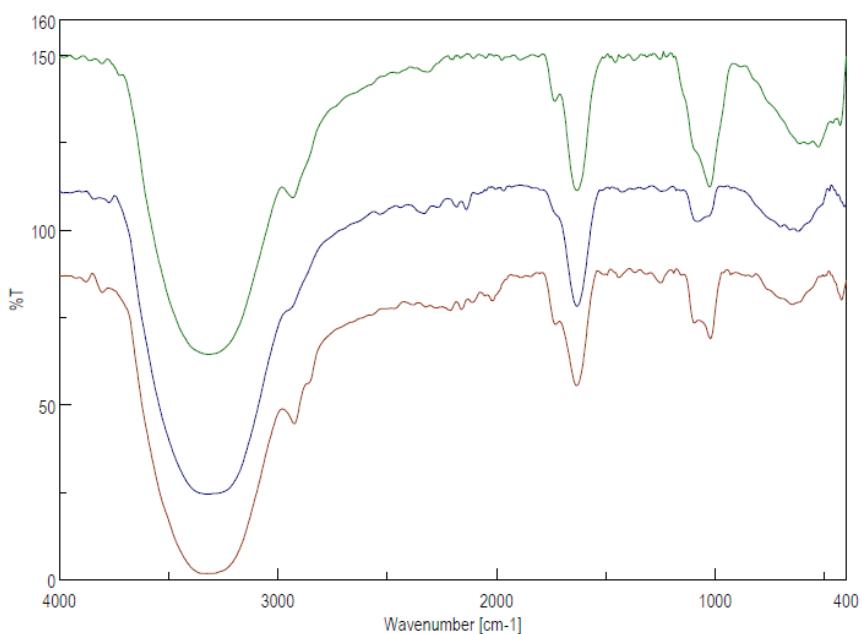


Figure 5. FT-IR results (the green line represents July, the purple line represents August, and the red line represents September)

Conclusions

In this study, fruit width, length and weight varied throughout the ripening process, and more consistent measurements were obtained in September. These results indicate that fruit quality is closely related to ripeness level.

When the changes in the $L^*a^*b^*$ values were analyzed, the L^* value reached the highest value in August. Value a^* was dominated by green tones in July, whereas in August and September, the value became positive, and red tones were dominant. The value of b^* was analyzed, and yellow tones were dominant in July and August. The value decreased in September and approached blue tones. Among the randomly measured fruits, high delta E values were obtained, whereas the July data showed sharp increases. Significant and irregular differences are likely to occur because of climatic conditions or conditions related to the growing environment of the fruit.

The Brix values steadily increased throughout the ripening process and reached the highest level in September. These findings indicate that fruit ripening is directly proportional to sugar accumulation.

Nine common volatile components (acetaldehyde, 2-propanone, hexanal, (E)-hept-2-enal, (E)-2-hexenal, (E)-2-hexen-1-ol, β -myrsen, simol, and limonene) were detected in the fruits. Changes in the concentrations of some components were observed between months.

FT-IR analysis revealed changes in the chemical structure of the fruits and provided information on the vibrations of phenolic OH groups. These results may reflect the climatic conditions to which the fruits were exposed during ripening.

As a result, this study contributes to the understanding of the biological and chemical properties of hawthorn fruit and emphasizes the importance of harvesting fruits at optimum ripeness. These findings indicate that hawthorn fruit may have potential for use in sectors such as food, pharmaceuticals and cosmetics.

Ethics Committee Approval

N/A

Peer-review

Externally peer-reviewed.

Author Contributions

Conceptualization, Investigation, Material and Methodology, Writing-Original Draft, Writing-review & Editing: F.M.N

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