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Mini Review
Bibliometric Analysis of Bio Fragrance from Carotenoid: From Pigment to Aroma Compound

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Abstract
Carotenoids are a class of naturally occurring pigments responsible for the vibrant colors in many fruits and vegetables. Beyond their well-known role in human nutrition and health, carotenoids hold untapped potential in a variety of industries, including cosmetics and fragrances. This study aims to explore the advancement of research related to the utilization of carotenoids for fragrance, specifically by analyzing bibliometric trends using the Crossref database and VOSviewer software. Sample articles were downloaded in RIS format obtained from Publish or Perish and then processed using a VOSviewer to visualize and analyze trends in the form of bibliometric maps. The data collected were 2000 papers in the period 2014-2024. The frequency of keywords can be adjusted as desired and less relevant keywords can be removed. By leveraging VOSviewer, the distribution of bibliometric maps is presented through three distinct visualizations: Network visualization, Density visualization and Overlay visualization. This bibliometric analysis reveals a diverse and interconnected landscape of carotenoid research. Analysis was conducted to see the potential of carotenoids in biofragrance. From the visualization, one of the small nodes is "carotenoid esters" which has a positive relationship with ionone, apocarotenoid and carotenoid cleavage dioxygenase. This highlights the potential of carotenoids in new applications such as biofragrance.

Key words: Degradation, essential oil, economics, bio-fragrance, carotenoid cleavage, bibliometric analysis

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INTRODUCTION

Fragrances and flavor are extensively utilized in industries such as food, feed, cosmetics, chemicals and pharmaceuticals[1]. The extraction of both volatile and non-volatile compounds from plants and animals has been practiced since ancient times and remains a fundamental process in creating aromas and fragrances, widely incorporated into formulations for the cosmetic, pharmaceutical and food industries[2]. Today, flavors used as additives in beverages and foods are primarily produced through chemical synthesis or extraction from natural sources. The distillation process is often used to extract fragrances from natural ingredients or crops[3]. However, plant-based extraction has several drawbacks, including low yields of the desired product, seasonal variability, susceptibility to plant diseases, compound stability issues and potential trade restrictions. There is a growing trend toward the bio-production and adoption of biologically derived flavor compounds, known as bioflavors and biofragrance[4,5].

The natural yield of fragrances from raw ingredients is typically only 1-3%, necessitating the use of large quantities of raw materials. To address this challenge, advanced process engineering technologies have been developed to produce fragrances without relying on natural extraction. Transforming secondary metabolites with high natural yields into aromatic compounds offers a promising solution. For instance, β-carotene from carotenoids can theoretically be converted into a precursor for producing aromatic compounds or fragrances with oxidation. This oxidation process can take place either naturally or intentionally[6-9].

Carotenoids are a class of naturally occurring pigments responsible for the vibrant colors in many fruits and vegetables, such as pumpkins, sweet orange potatoes, carrots and others[10]. Beyond their well-known role in human nutrition and health[11], carotenoids hold untapped potential in a variety of industries, including cosmetics and fragrances. It is widely recognized for its diverse applications and potential use in bio-fragrance development. These compounds, sourced from plants, algae and microorganisms, have garnered significant attention due to their sustainable and eco-friendly nature. In the context of biofragrance, carotenoids are promising candidates for producing aromatic compounds through natural degradation or biotransformation processes, aligning with the global shift towards green and innovative solutions in the fragrance industry.

One application is the development of carotenoid-based agricultural products as a novel source of rose fragrance. In theory, oxidation of carotenoid compounds can form aroma compounds like β-ionone and apocarotenoid. The β-ionone is a distinctive aromatic compound found in various flowers and fruits, including blackberries, peaches and apricots, among others. It is typically associated with a violet fragrance and a woody scent[12]. This oxidation process can occur naturally or intentionally[13]. Carotenoids have conjugated double bonds and an unsaturated structure, which leads to the formation of complex degradation products. This makes carotenoids highly prone to oxidation. Furthermore, storing carotenoid pigments in organic solvents can accelerate the decomposition process[14]. Apocarotenoids are products formed from the degradation of carotenoids, a process that can occur through enzymatic and non-enzymatic oxidative breakdown of carotenoids[15].

Instruments commonly used for the analysis of aromatic compounds from carotenoid degradation products include High-Performance Liquid Chromatography (HPLC), which is used for the separation and quantification of beta-ionone with high accuracy, often combined with UV-Vis detection to measure its absorption at specific wavelengths. Additionally, mass spectrometry (MS) is frequently used to analyze the molecular mass and structure of beta-ionone, while gas chromatography (GC), particularly when coupled with MS detection (GC-MS), is used for more volatile compounds[16].

This study aims to explore the advancement of research related to the utilization of carotenoids for bio-fragrance, specifically by analyzing bibliometric trends using the Crossref database and VOSviewer software. Bibliometric analysis is a crucial tool that enables researchers to map the landscape of scientific studies, uncovering patterns, collaborations and trends within the domain. This approach provides insights into the current state of research and highlights opportunities for further investigation and cooperation between stakeholders, including researchers, policymakers and industry leaders.

METHODOLOGY

All articles analyzed in this study were taken from the Crossref database, one of the peer-reviewed journal databases that can provide good scientific academic information. The study was conducted by conducting an online search from 1 September to 25 November, 2024, with the keyword "Fragrance of carotenoid" according to the criteria of "Title, Keywords and Abstract (topic area)".

Sample articles were downloaded in RIS format obtained from Publish or Perish and then processed using VOSviewer to visualize and analyze trends in the form of bibliometric maps. The data collected were 2000 papers in the period 2014-2024. The frequency of keywords can be adjusted as desired and less relevant keywords can be removed[17]. The VOSviewer can make publication maps, country maps, or journal maps based on networks (co-citation) or build keyword maps based on shared networks[18].

RESULTS AND DISCUSSION

Carotenoid production is the most frequently studied research area: The concept of bibliometric network visualization, also known as "science mapping", has been a major concern since the early development of bibliometric research. Visualization is considered an effective method for analyzing various types of bibliometric networks, such as citation relationships between publications or journals, collaboration networks between researchers and co-occurrences between keywords. One of the software that can be used for this analysis is VOSviewer[19].

Bibliometric mapping can be displayed by VOSviewer in three different visualizations: Network visualization, Overlay visualization and Density visualization. The colored circles represent each keyword, with varying circle sizes indicating the frequency of their occurrence. The more frequently a keyword appears, the larger the circle and font size will be. After being analyzed using VOSviewer, there are 7 clusters (red, green, blue, orange, dark blue, purple and yellow) that show the relationship between one topic and another. Clustering in bibliometric analysis is based on the number of co-occurrences or direct connections[17].

In Fig. 1, it can be seen that the large node sizes for terms such as "carotenoid production", "carotenoid biosynthesis", and "carotenoid accumulation" in the red and green groups indicate that these are the most frequently studied research areas. This reflects the primary focus of this field on understanding and improving carotenoid production. The emergence of terms such as "orange carotenoid protein" and "carotenoid esters" in the small groups (yellow and orange) indicates that this is a new area that is starting to develop.

Next, if analyzed in terms of clustering, the red cluster indicates research on how carotenoids are produced, the factors influencing their production and other characteristics. Meanwhile, the green cluster tends to focus on the biosynthetic pathways of carotenoids in specific organisms, including their genetic regulation and the role of enzymes such as phytoene in carotenoid synthesis[20]. It is mentioned that one potential approach for the mass production of carotenoids is through the use of engineered microorganisms. A deeper understanding of the carotenoid metabolic pathways in plants and microorganisms could open up new opportunities for the synthetic metabolic engineering of carotenoids and enhance the accumulation of carotenoids and their derivatives in various organisms.

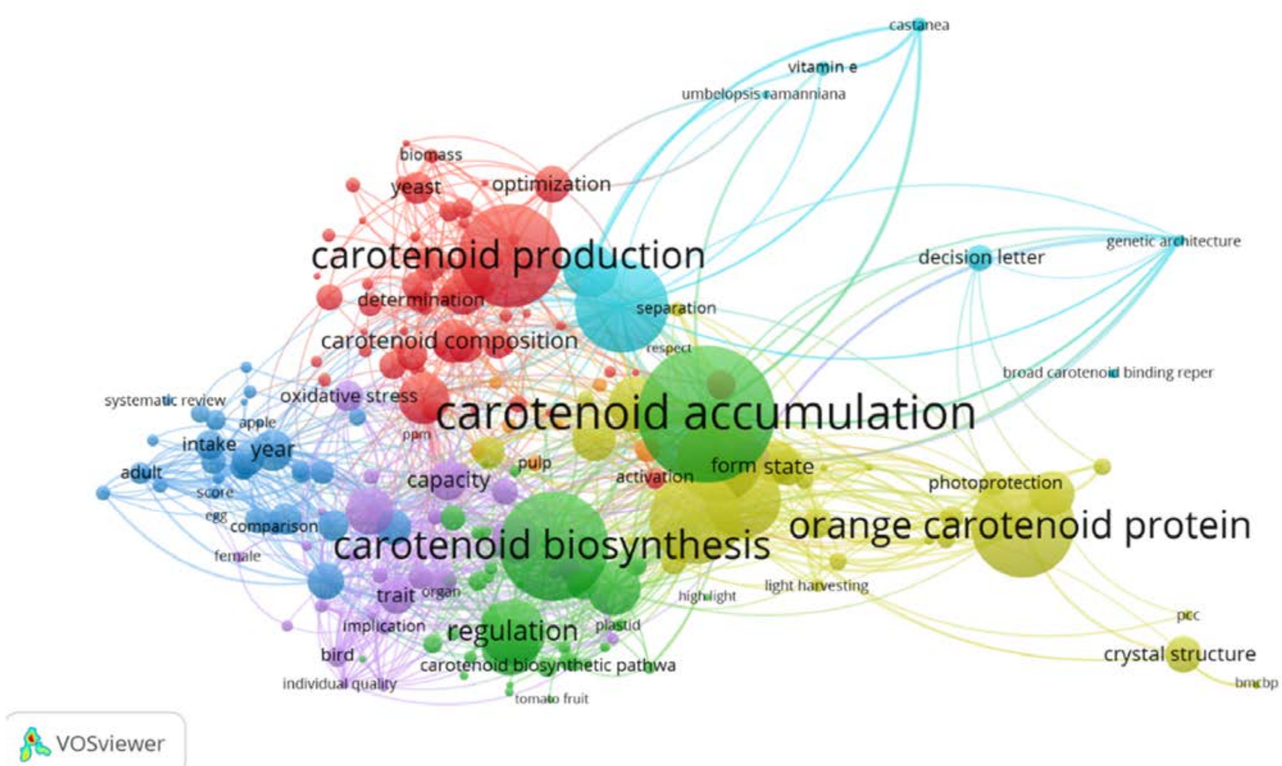

Fig. 1: Network visualization for research on carotenoids

The metabolic pathways in plants and microorganisms can be seen as a new opportunity for synthetic metabolic engineering due to their ability to enhance the efficiency of producing valuable compounds, such as carotenoids, in a sustainable and environmental friendly manner. By understanding and modifying these metabolic pathways, scientists can optimize the production process in plants and microorganisms through genetic engineering, allowing for improved yield and stability of the desired compounds. Additionally, the use of engineered microorganisms enables the production of compounds on a large scale at low cost, without relying on limited natural resources[21].

Carotenoid production is one of the most frequently conducted research themes. Carotenoids are obtained by various extraction methods like maceration[22], supercritical fluid extraction (CO^2 supercritical), ultrasound-assisted extraction[23], enzymatic extraction[24] and various types of solvents from various agricultural products such as carrots, corn, red sweet potatoes, pumpkins and even palm oil waste[25]. Various types of solvent extraction are used to obtain compounds from plants, including extraction with organic solvents such as hexane, ethanol, methanol, isopropanol and chloroform. In addition, supercritical extraction using carbon dioxide at high pressure and temperature is also a popular method for obtaining compounds with high efficiency and lower environmental impact[26-28].

Each type of solvent has its advantages and disadvantages depending on the chemical properties of the compounds to be extracted and the intended application[29]. The characteristic orange color of palm oil arises from these carotenes[30], with their concentration typically ranging from 400 to 3500 ppm. Palm oil contains approximately 15 times more retinol equivalents (vitamin A) than carrots and 300 times more than tomatoes. The extraction of carotenoids from various types of palm oil waste using several extraction methods with various types of solvents and the levels of carotenoids obtained can be seen in Table 1.

Meanwhile, the orange and yellow clusters encompass research on the function of orange carotenoid proteins in photosynthesis and cell protection from damage caused by excessive light[20]. Furthermore, the purple and dark blue clusters focus on the health benefits of carotenoids, including their impact on oxidative stress, prevention of chronic diseases and the bioavailability of carotenoids from food. Studies show that carotenoids offer significant health benefits, including acting as antioxidants that can reduce oxidative stress, prevent chronic diseases and enhance their bioavailability from dietary sources[31-33].

The light blue cluster analyzes the genetic structures underlying carotenoid synthesis and their relationship to phenotypes. This is related to studies utilizing genomic techniques to understand genetic variations affecting carotenoid biosynthesis[34]. This clustering can serve as a reference for research focus and areas that require further development to optimize the potential of carotenoids.

Table 1: Extraction system of carotenoids

Type of CPO waste	Method	Solvent	Conditions	Result	Source
Oil palm empty fruit bunch (OPEFB) spikelet	Soxhlet extraction	n-hexane	5 g of OPEFB and 300 mL solvent (1:60). Extraction process was carried out for about 3 hrs	2.32±0.01 ppm	Anshori *et al.*[35]
OPEFB	Soxhlet adsorption	IPA then hexane	Sample was extracted from the adsorbent with IPA for 1 hr. Then, followed by carotene extraction using hexane for about 3 hrs (adsorbent became colourless)	702 ppm	Kupan *et al.*[36]
Palm pressed fiber (PPF)	Soxhlet adsorption	IPA then hexane	Sample was extracted from the adsorbent with IPA for 1 hr. Then, followed by carotene extraction using hexane for about 3 hrs (adsorbent became colourless)	1414 ppm	Kupan *et al.*[36]
OPEFB sample size	Maceration	Hexane	Sample and hexane (1:20 w/w), duration for maceration 48 hrs	915.25 ppm	Manurung *et al.*[37]
Oil of the palm-pressed fiber (PPFO)	Solvent extraction	Hex and Hep: IPA	Solid: Solvent ratio 1:5 (by mass) for 8 hrs and at room temperature (25±1°C)	2539±78 mg β-carotene/kg PPFO	Alvarenga *et al.*[38]
Palm oil mill effluent	Solvent extraction and adsorption chromatography	Hexane and ethanol	Sample and hexane (1:0, 6) in a flocculator for 10 min at 350 rpm. For adsorption sample was eluted with n-hexane then ethanol and fraction were collected in the receiving flask	453 ppm	Ahmad *et al.*[39]
Palm oil mesocarp	Sub-critical extraction	R134a solvent	Yield of palm oil and the solubility of β-carotene were investigated at 40, 60 and 80°C and a pressure range from 45-100 bar	330-780 ppm	Mustapa *et al.*[40]
Crude palm oil	Supercritical extraction	CO_2 solvent	Pressure of 140 bar, temperature of 102°C and extraction time of 3.14 hrs	1.028×10^{-2}%	Davarnejad *et al.*[41]

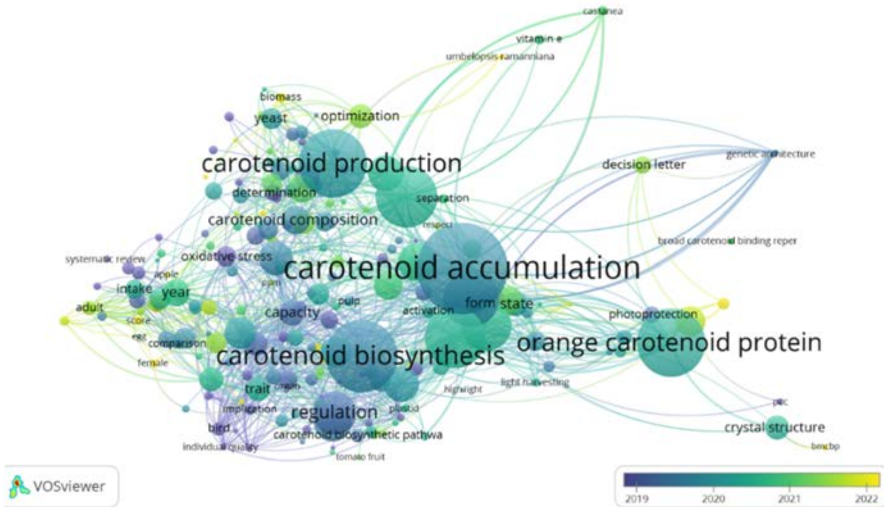

Fig. 2: Evolution of carotenoid research from fundamental aspects to new applications

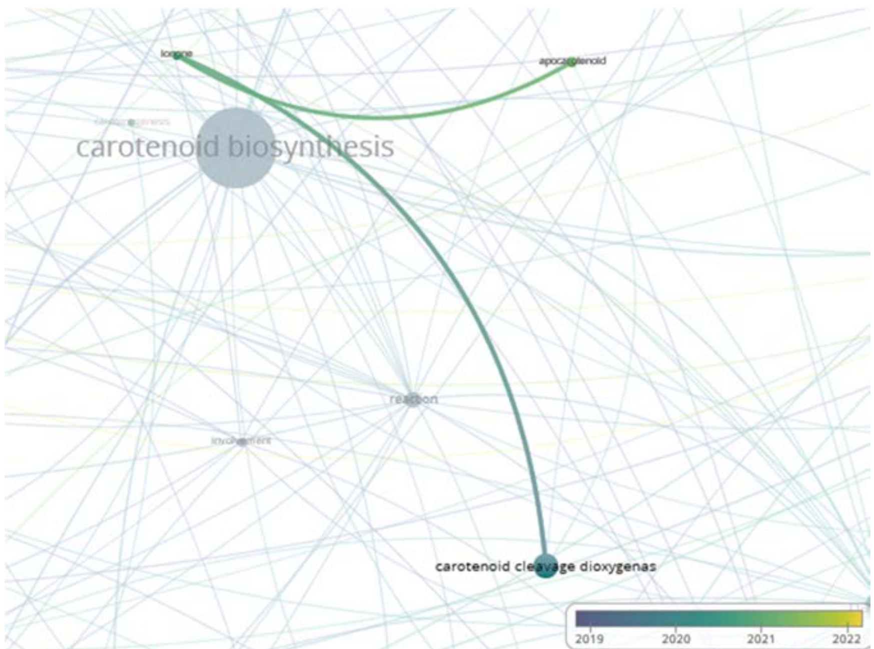

Fig. 3: Overlay visualization zoom out regarding carotenoid research

Potential carotenoids as biofragrance: The overlay visualization results show the evolution of carotenoid research from fundamental aspects to new applications. The colors and relationships between nodes illustrate how topics such as biosynthesis (blue), production (blue) and photoprotection applications (yellow) have evolved, with particular attention to new themes such as orange carotenoid proteins (yellow) and their use in innovative fields such as biofragrances. These results show the great potential of carotenoids to contribute to applied science and natural resource-based industries.

Further analysis was conducted to see the potential of carotenoids in biofragrance (Fig. 2) and it can be seen more clearly in Fig. 2. One of the small nodes (yellow) is "carotenoid esters" which has a positive relationship with ionone (bright green), apocarotenoid (bright green) and carotenoid cleavage dioxygenase (bright blue). This highlights the potential of carotenoids in new applications such as biofragrance. Meanwhile, the dark blue cluster focuses on genome editing technologies (e.g., CRISPR) that can be used to optimize carotenoid properties in organisms[20].

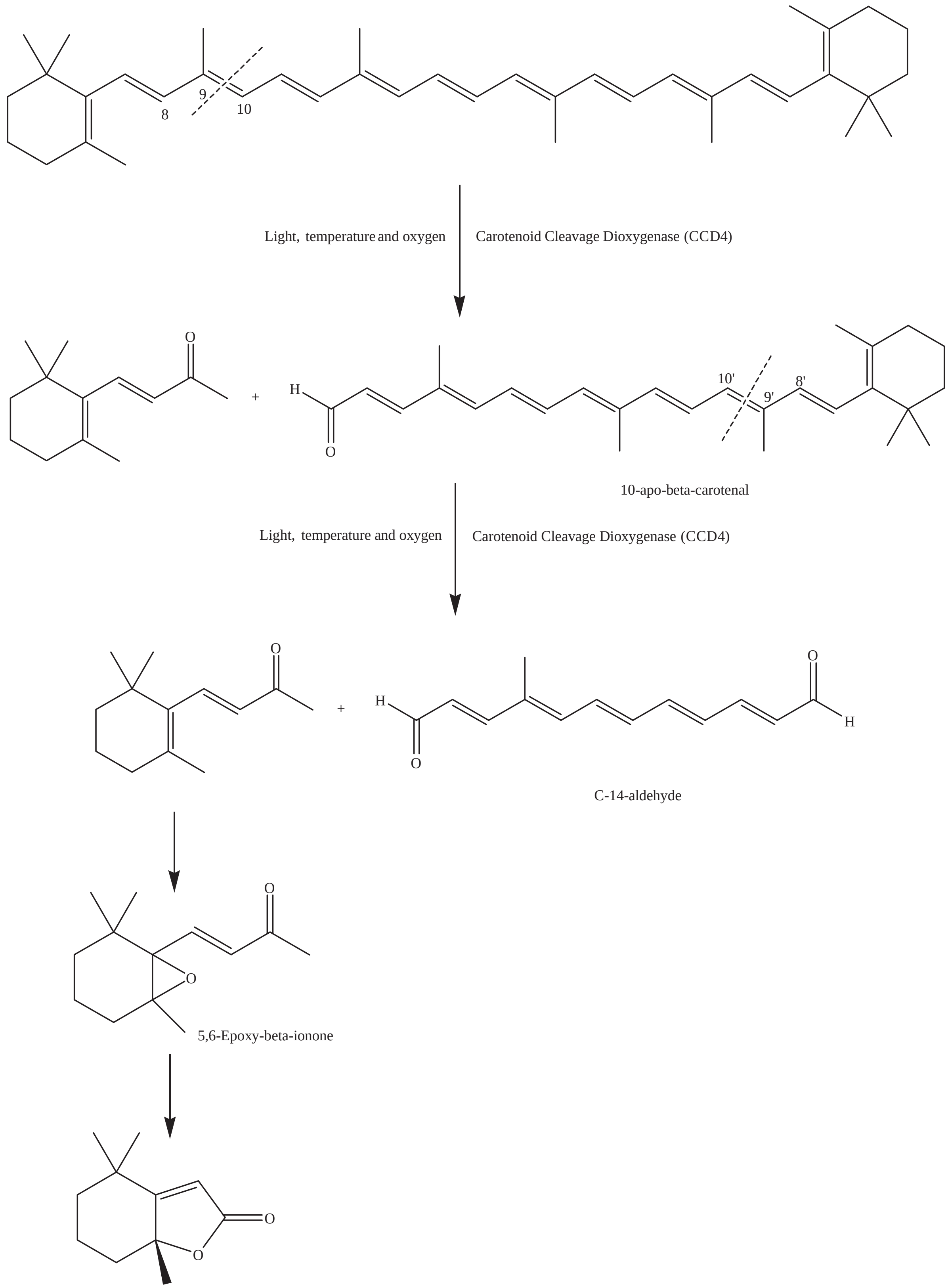

Fig. 4: Degradation of carotenoid pathway

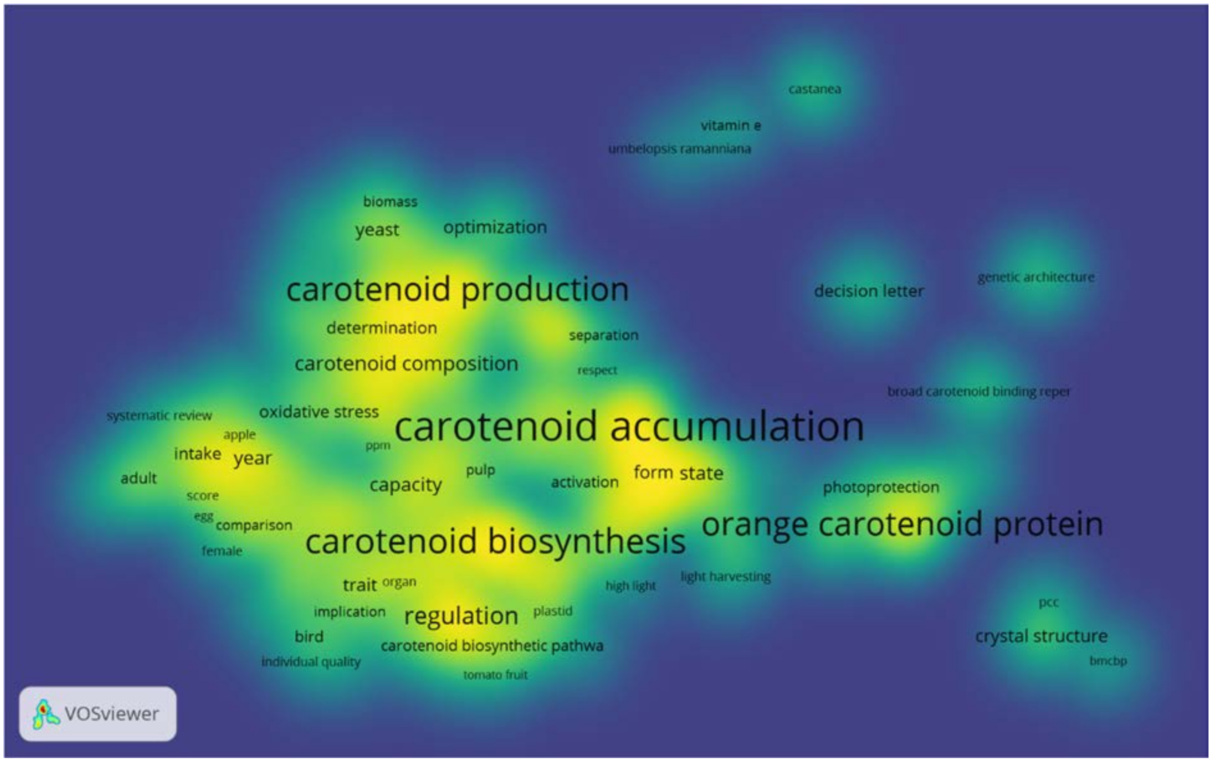

Fig. 5: Frequency density and relevance in the retrieved metadata regarding carotenoid

Carotenoids function as precursors of a large group of active compounds, namely apocarotenoids. The electron-rich polyene chains in carotenoids are very susceptible to oxidative damage. This leads to the formation of non-specific apocarotenoid products through random cleavage carried out by enzymes that are not related to carotenoids such as lipoxygenase or peroxidase. However, apocarotenoids are usually produced from biologically active processes, which are produced from specific enzymes, namely Carotenoid Cleavage Dioxygenase (CCDs) often referred to as Oxygenases (CCOs)[42]. The mechanism of carotenoid cleavage can be seen in Fig. 3.

Carotenoids can be broken down into apocarotenoids with the help of carotenoid can be divided into Nine-cis-epoxy carotenoid dioxygenase (NCEDs) and carotenoid cleavage dioxygenase (CCDs)[43]. The function of CCO from different subfamilies is very varied, including the CCD1, CCD2 and CCD4 subfamilies which are known to be involved in biosynthetic processes related to aroma, taste and color formation in apocarotenoids[44]. The NCED plays an important role in plant growth and development and is involved in the ABA biosynthesis process.

The function of the CCD1 and CCD4 subfamilies in carotenoid degradation products is the most studied in plants Fig. 4. The cleavage products are usually responsible for the volatile products. The CCD4 enzyme is located in plastids, its substrate specificity is generally higher than that of CCD1. CCD4 can cleave β-carotene, cryptoxanthin and zeaxanthin into apocarotenoids[45]. The CCDs usually catalyze the cleavage of non-aromatic double bonds by dioxygen and form aldehyde and ketone products. The CCD enzyme contains Fe^{2+} ions which function as a cofactor that is very necessary for cleavage activity. Its role is to activate oxygen which is involved in enzymatic reactions.

Density visualization (biofragrance): This density visualization shows keywords' frequency density and relevance in the retrieved metadata. Yellow indicates areas with high frequency (highly researched topics), while green and blue indicate topics with lower frequency or less attention in research can be seen in Fig. 5. "Carotenoid Accumulation" is in the center and is the topic with the brightest color (yellow), indicating that it is the most frequently researched theme and is closely related to many other keywords. The research focus on "carotenoid accumulation" covers how carotenoids are stored in organisms, such as plants, microorganisms or animals. This topic's existence in the center shows its relevance as a core discussion in this field.

CONCLUSION

This bibliometric analysis reveals a diverse and interconnected landscape of carotenoid research. The field ranges from basic studies on biosynthesis and regulation to applied studies on production optimization, health applications and innovative uses such as biofragrances and photoprotection. Mapping and clustering also reveal new trends and opportunities for future research, particularly in industrial and biomedical applications.

SIGNIFICANCE STATEMENT

This study reveals a diverse and interconnected landscape of carotenoid research. That can be beneficial for the development of research related to carotenoids from year to year. This study will help the researchers uncover the critical areas of new trends and opportunities for future research, particularly in industrial and biomedical applications that many researchers were not able to explore. Thus, a new theory on the potential of carotenoids in new applications may be arrived at.

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