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Formation and Inhibition of Cholesterol Oxidation Products (COPs) in Foods; An Overview

김주신†

신한대학교 보건대학, 식품영양학과전공
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식품 내 콜레스테롤 산화 생성물(COPs)의 생성 및 억제; 개요

Joo-Shin Kim†

Department of Food and Nutrition, Shinhan University
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Abstract : Cholesterol is prone to oxidation, which results in the formation of cholesterol oxidation products (COPs). This occurs because it is a monounsaturated lipid with a double bond on C-5 position. Cholesterol in foods is mostly non-enzymatically oxidized by reactive oxygen species (ROS)-mediated auto-oxidative reaction. The COPs are found in many common foods of animal-origin and are formed during their manufacture process. The formation of COPs is mainly related to the temperature and the heating time the food is processed, storage condition, light exposure and level of activator present such as free radical. The level of COPs in processed foods could reach up to 1-10 % of the total cholesterol depending on the foods. The most predominant COPs in foods including meat, eggs, dairy products as well as other foods of animal origin were 7-ketocholesterol, 7α-hydroxycholesterol (7α-OH), 7β-hydroxycholesterol (7β-OH), 5,6α-epoxycholesterol (5,6α-EP), 5,6β-epoxycholesterol (5,6β-EP), 25-hydoxycholesterol (25-OH), 20-hydroxycholesterol (20-OH) and cholestanetriol (triol). They are mainly formed non-enzymatically by cholesterol autoxidation. The COPs are known to be potentially more hazardous to human health than pure cholesterol. The procedure to block cholesterol oxidation in foods should be similar to that of lipid oxidation inhibition since both cholesterol and lipid oxidation go through the same free radical mechanism. The formation of COPs in foods can be stopped by decreasing heating time and temperature, controlling storage condition as well as adding antioxidants into food products. This review aims to present, discuss and respond to articles and studies published on the topics of the formation and inhibition of COPs in foods and key factors that might affect cholesterol oxidation. This review may be used as a basic guide to control the formation of COPs in the food industry.

Keywords : Cholesterol, Autoxidation, COPs, Processing, Storage

†Corresponding author
(E-mail: jskim@shinhan.ac.kr)

1. Introduction

Cholesterol is widely found in foods of animal origin. Cholesterol is easily oxidized to form COPs under certain food processing or storage conditions (1-2). COPs in cholesterol-containing foods have been found to be potentially hazardous to health. Dietary COPs have been well-known to have adverse health effects on consumers(3). COPs are known to have more devastating effects on arterial cells than pure cholesterol. Moreover, they show a direct link to atherosclerosis and coronary heart disease (CHD)(4). Additionally, COPs have been known to deteriorate the bioavailability of cholesterol by stopping cholesterol biosynthesis and dietary uptake of cholesterol(5-6). Potential undesired biological effects of COPs such as cytotoxicity, mutagenicity, carcinogenicity and cell membrane damage have been also suggested in numerous studies(7-8). The oxidation of cholesterol can occur both enzymatically and chemically. Even though the degree of COPs' formation in foods depends on the factors of food processing and most of COPs found in foods are subject to processing conditions or exposure to heat, the COPs in foods are mainly formed non-enzymatically by reactive oxygen species (ROS)-mediated autoxidation (9-10). As it is shown in Figure 1, cholesterol is a sterol lipid with a hydroxyl group on C3 and a double bond on C5. COPs are also a sterol group that are similar in structure. However, they contain an additional functional group, including a hydroxyl, ketone or an epoxide group in the sterol nucleus and/or on the side chain of molecules (11).

The most common COPs present in foods formed during autoxidation are 7-ketocholesterol, 7α-hydroxycholesterol (7α-OH), 7β-hydroxycholesterol (7β-OH), 5,6α-epoxycholesterol (5,6α-EP), 5,6β-epoxycholesterol (5,6β-EP), 25-hydoxycholesterol (25-OH), 20-hydroxycholesterol (20-OH) and cholestanetriol (triol). The chemical structures of these COPs are depicted in Figure 2. Many studies demonstrated that the number of COPs present in foods could often reach 1 % of the total cholesterol and in some cases amount to 10% or more (4). Foods such as meat products, dairy products and egg products, that are rich in cholesterol are prone to undergo cholesterol autoxidation and form COPs (12). COPs can also be produced during processing foods with exposure to heat, air, light and radiation, as well as, improper storage conditions also promote COPs formation (12).

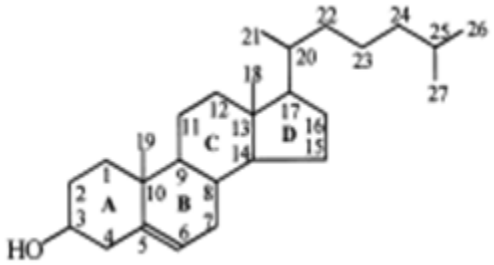

Fig. 1. The chemical structure of cholesterol.

As the consumption of processed cholesterol-rich foods is increasing, it is significant to clarify what implications COPs have when produced during food processing or during inappropriate storage, in order to reduce dietary COPs-induced health hazards. This review presents real insight into the most related areas concerning COPs in foods. It discusses the cholesterol oxidation mechanism and processing factors including storage conditions that affect the formation of COPs in foods. Moreover, COPs found in commonly consumed food products and their inhibition mechanism are described.

The goal of this study is to examine the mechanisms of COPs' formation in various foods, the major components that contribute to COPs' production, and the inhibition mechanisms of COPs, and to explore the major COPs in commonly consumed cholesterol-containing foods. Previous studies

were reviewed to understand the mechanisms and facilitating factors of cholesterol oxidation. The production patterns of major COPs in foods of animal origin that contains high level of cholesterol were described by collecting recent research trends and utilizing literature review method to describe the data according to the need and purpose of the study.

2. Mechanism of cholesterol oxidation

Cholesterol is one of the main sterols found in animal tissues. It is a high molecular weight alcohol sterol which is one of major components of the nonsaponifiable fraction of oils and fats (13). Cholesterol can appear in the free form. It may also be combined with long-chain fatty acids or appear as cholesterol esters. This enables it to be an essential structural component of membranes and plasma lipoproteins, in fluidity modulation, as well as playing the role as a precursor in the synthesis of steroid hormones, bile acids and vitamin D_3(13-14). As shown in Figure 1, cholesterol consists of four fused rings. They

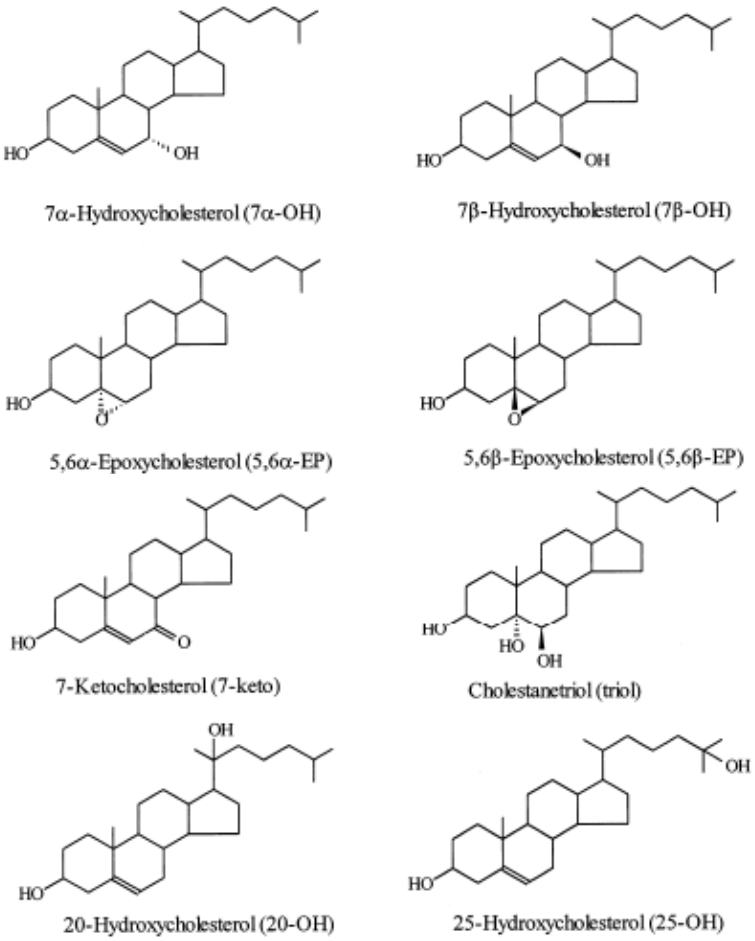

Fig. 2. The chemical structures of COPs found in foods.

are aliphatic side chain split to the D-ring at the C-17 position, a hydroxyl group connected to the A ring at C-3 position, and a double link between C-5 and C-6 positions of B ring. Because cholesterol is a molecule with an unsaturated or double bond, it is prone to oxidation. Therefore, cholesterol is sensitive to free radical oxidation by diatomic molecular oxygen (O_2) in the presence of oxygen (15). While the vulnerability of cholesterol to oxidation has been explored and studied for over a century, it is still not perfectly clear how COPs are formed (2).

Cholesterol oxidation has been known to be similar to the mechanism of lipid oxidation. It is reported that cholesterol oxidation can begin at a high temperature when oxygen is present or under light, resulting in autoxidation (15). Based on the study described by Otaegui-Arrazola et al. (10), cholesterol in foods is mainly oxidized non-enzymatically by an ROS-mediated auto-oxidative reaction (10). ROS related to cholesterol oxidation in foods consist of various radical molecules including hydroxyl ($^{\cdot}OH$), peroxyl (ROOH), and superoxide ($O_2^{\cdot -}$) radicals, and non-radical molecules, such as hydrogen peroxide (H_2O_2), singlet ($^1O_2$) and triplet ($^3O_2$) oxygen, and ozone (O_3) (16). These species can be produced enzymatically, chemically, or photo-chemically under different food processing and storage conditions. They also decompose or interact with each other to generate other radical species(17). ROS generated during food processing attacks cholesterol molecule, forming a variety of COPs. COPs are part of a group of sterol that share a similar structure with cholesterol. However, an additional hydroxyl, ketone or epoxide group consists in the sterol nucleus, or it contains a hydroxyl group shown on a side chain of the molecule (13).

Generally, cholesterol oxidation can be initiated by abstraction of hydrogen. It occurs predominantly at C-7 position of a cholesterol molecule, followed by the addition of an oxygen molecule. This leads to the formation of 7α-hydroperoxycholesterol (7α-OOH) or 7β-hydroperoxycholesterol (7β-OOH), the primary oxidation product during heating (Figure 3). The reduction of 7α-OOH and 7β-OOH further results in formation of 7α-OH and 7β-OH, that can be widely found in foods (4). Isomeric 7-hydroperoxycholesterol can also undergo dehydration during heating and form 7-ketocholesterol, which is also a key result of autoxidation of cholesterol in the food system (13). Additionally, 7-ketocholesterol can be an outcome of dehydrogenation of the isomeric 7-hydroxycholesterol in the presence of radicals (18). Under basic conditions, 7-ketocholesterol can be converted to 3,5-choleasta-dien-7-one and other compounds (19). Another group of COPs, 5,6α-EP and 5,6β-EP are also identified as products of cholesterol oxidation in foods by air, although its reaction mechanism is complex. The degrees of stability of 5,6-epoxides rely on the medium and the pH (20). Maerker and Bunick (21) reported that the ratio of 5,6α-EP/5,6β-EP was influenced by pH of the dispersion, since β-epoxide was hydrolyzed faster than α-epoxide. The isomeric 5,6-EP may also be hydrated under an acidic condition to form 3,5,6-cholestanetriol called triol, which is considered to be the most toxic. However, with the direct attack of cholesterol by singlet or triplet oxygen, only hydroperoxides are formed, not epoxides (19). The side chain oxidation of cholesterol may also occur and the oxidative attack at tertiary C-20 and C-25 position generate 20-hydroperoxycholesterol (20-OOH) and 25-hydroperoxycholesterol (25-OOH), respectively. These hydroperoxides can be further broken down to 20-OH and 25-OH. These are proven to be more stable and can endure consecutive heating at 100℃ for 6 months (15). The formation pathways of described COPs are summarized in Figure 3.

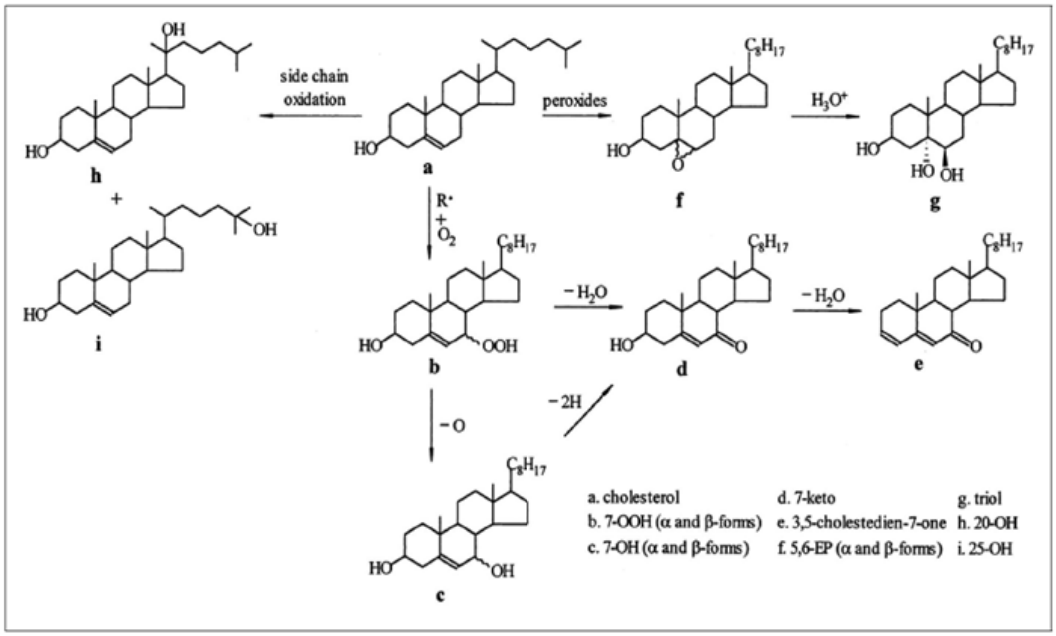

Fig. 3. The formation pathways of cholesterol oxide products during autoxidation described by Tai et al.(2).

3. Factors of cholesterol oxidation

Most dietary COPs form during food processing and storage. Therefore, detailed understanding on effects that food processing and storage conditions have on the formation of COPs is critical in developing strategies for reducing COPs. Many foods have been analyzed according to the level of cholesterol contained in them, as well as exposure to conditions that promote oxidation of cholesterol. Heat application, light exposure and duration of storage are some of the conditions. The amount of COP formation is dependent on the temperature and length of heating time as well as the storage conditions, level of activator present and exposure time of light (22-23).

3.1. Temperature and time

Cholesterol oxidation is promoted by the production of free radicals, that is a result of energy that is provided by heating to overcome the activation energy of hydrogen abstraction (17). Overall result from several sources suggested that no COPs were found in fresh food. The foods most oxides were detected were those that underwent the processing conditions or exposure to heat. Cooking cholesterol-rich foods increased the production of COPs. Also, the rate of cholesterol oxidation in foods was greatly accelerated during storage after cooking. It was found to show the same trend as lipid oxidation (1). Park and Addis (24) reported that cholesterol was oxidized to isomeric 7-OH, 7-ketocholesterol and 5,6-EP in beef tallow heated at 155℃ for 376 h. 7-Ketocholesterol was produced without formation of isomeric 7-OH as a decomposition product of 7-hydroperoxides. This is because 7-OH was immediately dehydrated at temperatures as high as 155℃ due to lack of water. Thermal decomposition of 7-hydroperoxides has been reported to bring about stable autoxidation products, like

7α-OH, 7β-OH and the dehydration product, 7-ketocholesterol. The formation of 7-ketocholesterol showed a nearly linear relationship with heating time (24). Derewiaka (25) reported that when the temperature increased from 150℃ to 180℃, heating cholesterol for 1 h leads to cholesterol loss from 64.1% to 90.5%. Barriuso et al. (26) established a degradation curve of cholesterol which showed that 79.6% of cholesterol have degraded at 180℃ after 90 min. According to the study of Min et al. (27), heating 50mg cholesterol at 100℃, 150℃, and 200℃ for 1 h yielded 0.11, 2.60, and 1.33mg COPs (7β-OH, 20-OH and 25-OH; triol, 5,6α-EP; and 7-ketocholesterol), respectively. However, heating cholesterol at 120℃ for 30, 60, 120, and 180 min in closed ampoule did not result in the formation of COPs and only showed 12.2-13.9% of cholesterol loss (28). Heating cholesterol at 150℃ generated the highest content of COPs compared over the same duration of time (29). The amount of COPs formed during oxidation of cholesterol was not equal to the cholesterol loss. However, overall, with the increase of heating time and temperature, the content of COPs formed showed an upward trend.

3.2. Light exposure

Cholesterol oxidation can also lead to the formation of various COPs during exposure to light. Generally, cholesterol reaction through photo-oxidation includes type I mediated by free radical and type II mediated by singlet oxygen (30). The type I reaction involves free radical that is formed by triplet sensitizer-reducing substrate interactions to form 7α-OOH/7β-OOH and further 7α-OH/7β-OH and 7-ketocholesterol. On the other hand, type II reaction relates to the $^1O_2$ formed by triplet sensitizer-ground state oxygen interactions to form 5,6α-EP/5,6β-EP and triol (30). Various studies have investigated the formation of COPs during food processing and storage under light exposure (31-33). The main factor of the efficacy of each reaction type are the relative concentrations of oxygen and substrate. The formation of COPs in soybean oil containing chlorophyll mainly depends on the type II reaction, while the photo-oxidation of cholesterol in water-based foods such as milk mainly depends on type I reaction (32). This is because oxygen is more soluble in nonpolar lipids than in water. Furthermore, the formation of COPs in foods under light exposure is closely related to the exposure time and light energy. Based on the study described by Boselli et al. (34), the level of COPs' formed in turkey breast in under the daylight fluorescence lamp with exposure at 6000 K reached their maximum in only 1 d, whereas it took up to 5-6 d for COPs to reach their maximum under a warm tone light at 3000 K. Overall, the level of COPs formed during food processing and storage under light exposure increases with longer light exposure time.

3.3. Storage condition

Foods are usually stored at relatively low temperatures. Given that the oxidation of cholesterol in food products occur slowly at low temperatures, longer storage times may lead to the production of COPs (35). Therefore, effects of storage time on the formation of COPs have been investigated in many studies. It can be concluded from most of the studies that when stored for a long duration of time, the content of COPs in foods keep increasing or/and then they stabilize. Of note, buttermilk stored at 3℃ can show formation of COPs only after 10 h (36). However, a relatively prolonged time of storage may show different trends. According to the study reported by Rather et al. (37), in canned goshtaba (an indian food) with 10% or 20% fat stored at 20-30℃ for 18 months, the levels of 7β-OH in samples showed an upward trend in the first 9 months and then were stable in the next 9 months. However,

levels of 7-ketocholesterol in the sample with 20% fat increased by 114.3% during the first 6 months and decreased by 32.8% in the following 12 months. Mechanism of degradation of 7-ketocholesterol during long-term storage is still unclear. Generally, the content of COPs in raw meat products is essentially zero before storage (24). However, the length of storage time must affect the formation of COPs in foods. According to the study by Conchillo et al. (38), total COPs levels in aerobically stored meat were 1.6-, 5.9- and 1.94-fold higher compared to vacuum-stored raw, grilled and roasted samples respectively. The efficacy of vacuum sealing while storing the meat in a freezer was proven to be higher for cooked than for raw samples in lowering cholesterol oxidation. The meat samples that showed the highest amounts of COPs were the cooked meats that were stored aerobically, especially the roasted samples. This result is evidence that shows cooking promotes cholesterol oxidation during storage (38). Even though the formation trends of some COPs may be different according to the storage condition, it is a significant factor in the formation of COPs in foods. Overall, with the increase of storage time, the content of COPs in processed foods is increased.

4. Cholesterol oxidation products in commonly consumed foods

4.1. Meat-based products

Lean meat consists of an average 10% of lipid on wet weight basis. Triglycerides and phospholipids are the key components while cholesterol takes up a smaller part, ranging from 50 to 89 mg (1). However, cholesterol present in meat product is subject to oxidation when exposed to processing and storage procedure that can compromise the nutritional properties. This results in non-enzymatically formed COPs. Particularly, 7-ketocholesterol has received much attention because at relatively high concentration it might induce a cytotoxic effect and play a role in the pathology of a variety of diseases (39). According to a study there were no significant differences in the 7-ketocholesterol content in different cooking treatments, however, the initial 7-ketocholesterol level in the raw meat were already shown to be quite high at 3.5 ppm (40). This might be an immediate result of the holding period, in which most meat is often kept at 4-6 °C for 10-15d to increase tenderness and promote flavor formation (40). Based on the report by Conchillo et al.(38), β-epoxycholesterol such as 5,6-β-EP was the most abundant COPs in raw chicken samples and in grilled chicken that were vacuum-stored. Meanwhile, the most COPs found in roasted chicken samples was 7-ketocholesterol. According to the study of Baggio et al. (41), 330 mg/kg of 7-ketocholesterol were found in raw turkey breast sample after 16 months in frozen storage. Amounts of 7α-OH, 7β-OH, 25-OH and 5,6-β-EP were found to be lower in vacuum-stored compared to aerobically stored samples. It is probable that the lack of oxygen under vacuum inhibited oxidation of cholesterol. (38). Kim (42) demonstrated that the rate of cholesterol oxidation in food system is greatly accelerated during storage after processing and appears to follow the same trend as general lipid oxidation. A report suggested that the predominant species was 7-ketocholesterol, which accounts for nearly half of the total COPs. It followed by 7α- and 7β-OH and both 5,6α/β-EP in order of decreasing concentration (43). Overall, even though fresh meat and fresh meat products show none or hardly any COPs, the production of COPs is significantly increased during food processing and storage. Among the COPs formed during food processing and storage in meat-based products, 7-ketocholesterol is the predominant product caused by cholesterol oxidation.

4.2. Milk-based products

There are estimated 12 mg cholesterol / 100g or 3 mg/g milk fat in milk and the content depend on several processing factors, and some dairy products are reported to contain COPs (1). Generally, COPs such as 7 β-OH, 7-ketocholesetrol, 25-OH, 27-OH, 5,6α/β-EP of non-enzymatic origin are also found in milk, mostly originating from the type of feeding, and processing and storage (39). Especially, among several COPs formed non-enzymatically, 7β-hydroxycholesterol described by 7β-OH and 7-ketocholesterol are most abundant in milk-based products and they account for around 86-88% of total non-enzymatic COPs found in milk-based products (39). According to the study by Risso et al. (39), non-enzymatic COPs in whole milk power increased significantly over time opposed to the product's freshness. Whole milk powder stored for 20 days contained a total of 449.2 ± 15.2 ng/g non-enzymatic COPs. In milk powder stored for 120 and 180 days, the amount increased to 626.8 ± 10.2 (1.4-fold increase) and 882.9 ± 22.9 (2-fold increase), respectively. Based on the research of Pikul et al. (44), the total contents of COPs in raw bovine and caprine milk amounted to 50 and 38 ㎎/100mL. However, regardless of the type of milk, a significant increase in total amounts of COPs was observed during storage of ultra-high temperature (UHT)-treated bovine and caprine milk. After the UHT bovine milk was stored for 6 months, the contents of COPs increased to 217 and 248 ㎎/100mL in milk stored at 4℃ and 20℃, respectively. In caprine milk the amount of COPs increased to 160 and 249 ㎎/100mL in the same condition. Among the COPs of non-enzymatic origin, especially 7α/β-OH, 5,6α/β-EP and triol increased significantly over time during storage (44). Generally, the amount of COPs present in milk-based products depends on the processing temperature and length of the storage period.

4.4. Egg-based products

An egg generally contains 213 ㎎ of cholesterol. Egg products show little concentrations of total COPs, ranging from trace amount to 200 ppm, however, there have been no COPs reported in fresh eggs (1). Like meat-based products and milk-based products, egg-based products generate a variety of non-enzymatic COPs during food processing and storage. 5,6α-Epoxycholesterol described as 5,6α-EP and 5,6β-epoxycholesterol described as 5,6β-EP in egg products have been reported as the most predominant oxidized cholesterol (4). According to a study, 5,6α-EP was a main accumulating product of cholesterol oxidation while egg powders were stored (45). The average levels of COPs in eggs were shown as follows, from high to low: 5,6α-EP, 7β-OH, 5,6β-EP and 7-ketocholesterol (45). Generally, cholesterol content in moisturized powders were lower than in dry ones. Based on the study of Obara et al (46), the total level of COPs was found to be higher in spray-dried powders compared to the freeze-dried ones. Water content in powders had significant influence on COP accumulation during storage (46). The estimation is that five COPs of spray-dried powder and 5,6α-EP content most accumulated in egg powders depending on the level of water. Before storage, 5,6α-EP constituted 37% of total COPs in egg powders, but after 3 months of storage, the 5,6α-EP content increased to 47% of total COPs (46). Caboni et al. (47) reported that the COPs content in spray-dried egg samples significantly increased during storage and the main COPs found in egg samples during storage were 7α/β-OH, 5,6α/β-EP, 7-ketocholesterol and triol. However, even though 7-ketocholesterol increased during storage, it represented only 10% of total COPs formed during storage unlike other non-enzymatic COPs. 7-ketocholesterol is the predominant COPs formed during storage in meat-based products, however, it is not the

main COPs in egg-based products. Overall, although 7-ketocholesterol might be the most predominant COPs formed in meat and milk-based products, it may be not in egg-based products and the COPs in egg products depend on the food processing method used for egg products.

5. Inhibition of cholesterol oxidation products

In view of potential harm COPs has on human health, efforts to prevent or reduce COPs consumption are currently being made. Since the main dietary sources of COPs are processed foods of animal origin that have high level of cholesterol, the prevention of COPs' production during food processing, storage, or culinary preparation, is of importance. As oxidation of both poly-unsaturated fatty acids (PUFA) and cholesterol proceeds through a free radical mechanism, and oxidation of cholesterol, like lipid, is enhanced with oxygen in high temperature, compounds that inhibit PUFA oxidation may also inhibit cholesterol oxidation (42). Therefore, the incorporation of antioxidants into foods containing high level of cholesterol may effectively help in slowing the oxidation. Both synthetic or natural antioxidants, are widely used to prevent lipid oxidation in processed foods, raw materials, or fats and oils used in manufacturing (48). However, even though antioxidant acts to prevent or delay PUFA oxidation, the effect of antioxidants to prevent COPs' formation is yet to be further investigated. Antioxidants are organic lipid or water-soluble substances that can detect the active forms of oxygen involved in the initial step or break the oxidative chain reaction (49). Antioxidants may react with the peroxy radicals induced from lipid to form stable antioxidant radicals. They are either immune to further reactions or result in non-radical products (49). Synthetic antioxidants mainly used in human foods are tertiary 2,6-di-tertiarybutyl-4-methylphenol (BHT), teritia-rybutyl-4-hydroxylanisole (BHA), tertiary butyl-hydroquinone (TBHQ), and the n-propyl ester of 3,4,5-trihydroxybenzoic acid (propyl gallate, PG) (48). Natural antioxidants, which can be found in different amounts in vegetables, fruits and grains, have gained a prominence as alternative to synthetic antioxidants due to health safety (49). The most beneficial antioxidant in slowing cholesterol oxidation has been proven to be α-tocopherol. It has shown better activity than other antioxidants, such as BHA or BHT (50). Csallany et al. (51) have demonstrated that α-tocopherol, BHA, and BHT are effective in stopping cholesterol oxidation when superoxide anion, water, and hydrogen-peroxide are present. Valenzuela et al. tested the effect rosemary extract has on cholesterol oxidation by utilizing highly purified soybean oil as the substrate for oxidation (52). The study showed that rosemary extract exerted a strong antioxidant effect by preventing both soybean oil oxidation and cholesterol oxidation (52). Janoszka (53) conducted a study on onion and garlic and their effectiveness on the formation of 7-ketocholesterol and 7-OH. It was proven that adding 30 g of onion to 100g meat product resulted in a significant decrease in 7-ketocholesterol and 7-OH concentrations by 79%. At the same time, when 15 g of garlic was added to 100g of meat product it was shown to lower the concentrations by 88%. Another study indicated the effectiveness of sage in controlling oxidation in lipid and cholesterol and minimizing the pro-oxidant effects of salt, cooking, and storage (54). Recently, strong evidence indicated that anthocyanin in Montmorency tart cherries may have a dose-dependent antioxidant activity, specifically targeting COPs (55). The emphasis on natural antioxidants is s response to concerns about the potential toxicity of synthetic antioxidant. Moreover, there are research findings that indicate a correlation

between active dietary ingredient, such as natural antioxidants, and their protection against various diseases caused by stress on the human body from free radical-induced oxidative.

6. Conclusions

This review has addressed the formation and inhibition mechanisms of COPs in foods, as well as the main factors influencing their formation. The COPs pose potential harm to human health. These products are generated from cholesterol-containing foods during processing and storage. High temperature, long time and light applied in different stages of food manufacture play a significant role in the process. Generally, the COPs in foods is mainly formed non-enzymatically by ROS-mediated autoxidation. Some COPs found in foods have undesired biological activity such as cytotoxicity, mutagenicity, carcinogenicity and cell membrane damage. Therefore, it is as equally necessary to make effort to stop COPs' formation during the food processing and storage as to identify COPs in foods that can be dangerous. It is clear that COPs' production can be reduced or minimized by focusing on their production means and factors that are responsible. Several measures can be adopted to lower the production of COPs in foods. The formation of COPs in cholesterol-rich foods can be minimized by lowering processing temperatures, minimizing processing, using oxygen-proof packaging and protective environment. Low-temperature and light-free storage may also be beneficial. Moreover, since cholesterol oxidation occurs through a free radical mechanism, as do lipid oxidation, the compounds used to inhibit lipid oxidation can be possible options in preventing or diminishing cholesterol oxidation. Even though the use of both synthetic and natural antioxidants may allow the protection of the formation of COPs, the emphasis given to natural antioxidant results from the concerns on toxicity of synthetic antioxidants. This review paper provides the basic information on the formation and inhibition pathway of COPs formed during food processing and storage, and key factors that might influence cholesterol oxidation. However, there are limitations in fully understanding the types and levels of COPs, which depends on the processing type and food matrix as well as cholesterol. Therefore, it is vital to further the research in investigating the relationship between the formation of COPs and food processing type or food matrix in the future.

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