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Review article

MCPD fatty acid esters in vegetable oils: formation, analysis and toxicology

Maryam Azizi-lalabadi[a], Mir-Michael Mousavi[b], Zahra Piravi-vanak[c], Sodeif Azadmard-Damirchi[d,*]

[a] *Research Center for Environmental Determinants of Health, Kermanshah University of Medical Sciences, Kermanshah, Iran*
[b] *Student Research Committee, Department of Food Science and Technology, National Nutrition and Food Technology Research Institute, Faculty of Nutrition Science and Food Technology, Shahid Beheshti University of Medical Sciences, Tehran, Iran*
[c] *Faculty of Food Industries and Agriculture, Standard Research Institute-ISIRI, Karaj, Iran*
[d] *Department of Food Science and Technology, Faculty of Agriculture, University of Tabriz, Tabriz, Iran*

A B S T R A C T

3-monochoropropane-1, 2-diol (3-MCPD) and 2-monochloropropane-1,3-diol (2-MCPD) and glycidol esters (GE) have been known as food contaminants. These compounds are formed during high-temperature process of different food products such as coffee, edible oils, infant formula, potato based products, bakery products, malt, cooked meats, soy sauces and pickles. In vegetable oils, these compounds are formed during refining, particularly during deodorization step. The studies on MCPD content and their formation routes in vegetable oil are a new area of research. Carcinogenic characteristics of these ingredients are a general concern. Thermal processing such as deodorization and deep-frying can trigger the formation of unpleasant substance such as trans fatty acids cyclic fatty acid esters, or acylglycerol polymers. Refining of edible oils, although eliminates contaminants from the oil, but it leads to the formation of unwanted compounds such as glycidol, glycidol esters, MCPD and MCPD esters. This review gives valuable information of present knowledge on analytical aspect, formation mechanisms of 3-MCPD and GE in vegetable oils and their health implications such as toxicity, carcinogenicity and mutagenicity.

Keywords: 3-MCPD esters, Food contaminant, Deodorization, MCPD analysis, Vegetable oil

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1. Introduction

Vegetable oils are composed of major components, triacylglycerols and minor components such as tocopherols, sterols, pigment and etc (Damirchi et al., 2005). However, some contaminants can also present in vegetable oils. These contaminants can be form in the oil through environmental pollution or different processing (Kamikata et al., 2019).

Unrefined edible oils may have different types of contaminants depending on its type, including hydrocarbons, residue of pesticides, dioxins, heavy metals, mycotoxins and etc. (Table 1) (Gibon et al., 2007; Wake, 2005). The main disadvantages of these substances are damages to oil quality, adverse effects on oil processing and hazardous to consumer health (Bockisch, 1993; Wong et al., 2019). Main aim of edible oil refining processes is separation or reducing these contaminants as much as possible. Generally, refining process includes degumming, neutralization, bleaching and deodorization. Among these steps, deodorization is done at high temperature (180-260 ºC) (Azadmard-Damirchi et al., 2008).

Chlorinated propanols such as 3-monochoropropane-1,2-diol (3-MCPD) (Fig. 1) and 2-monochloropropane-1,3-diol (2-MCPD) (Fig. 1) have been known as food contaminants produced during high-temperature treatment and processing of variety food products. These contaminants are detected in various food processing including smoked foods, meat (Crews et al., 2002; Kuntzer et al., 2006) cereal-derived foods (Hamlet Sadd et al., 2002) coffee, (Dolezal et al., 2005) French fries, (Svejkovska et al., 2004) bread, (Breitling-Utzmann et al., 2003; Starski et al., 2013) salty crackers, (Svejkovska et al., 2004) raw goat milk, (Cerbulis et al., 1984) biscuits, snacks and Chinese pastry (Chung et al., 2013) and etc. Velisek et al. (1978) was discovered 3-MCPD compound in soy sauce produced during acid-hydrolisation.

3-MCPD is a viscous liquid with racemic mixture of its enantiomers (Dolezal et al., 2002; Hamlet et al., 2004). These enantiomers have different toxicological effects such as antifertility activity, adverse impact on kidneys and *in vitro* genotoxicity effects (Dolezal et al., 2002; Lynch et al., 1998). Toxicological investigations confirmed the carcinogenicity of 3-MCPD in animal trainings and might malfunction of certain organs and induce infertility (Bakhiya et al., 2011; Barocelli et al., 2011; Liu et al., 2012; Yan et al., 2018). There were some investigations on the

*Corresponding author.
E-mail address: s-azadmard@tabrizu.ac.ir (S. Azadmard-Damirchi).

toxicological aspects of 3-MCPD esters as well (Bakhiya et al., 2011; Buhrke et al., 2011; Schilter et al., 2011). 3-MCPD was recognized as possibly carcinogenic to humans by organization of International Agency for Research on Cancer (IARC) (Humans, 2013). The Joint FAO/WHO Expert Committee on Food Additives (JECFA) (JECFA, 2016) established a tolerable daily intake (TDI) 2 µg/kg body weight for 3-MCPD (Beekman et al., 2018).

Furthermore 2-MCPD has also been reported in several foodstuffs, which accounts one third of the total MCPD ester content (Larsen, 2009). However, its toxicological properties is not clear, because of the very few toxicological data existing (MacMahon et al., 2013; Schilter et al., 2011).

The MCPD esters can be produced in a great range of food products and removing of this component from daily diet is impossible. The finding of 3-MCPD esters is important because the German Federal Institute for Risk Assessment (BfR) (fur Risikobewertung, 2007), supported by the European Food Safety Authority (EFSA) (Authority, 2008), assumes a 100% metabolism of the 3-MCPD esters to free 3-MCPD for which a tolerable daily intake - of 2 µg/kg body weight per day was defined. That means that by the consumption of refined fats and oils or foods based on refined fats and oils the TDI can be exceeded. Based on this assumption BfR recommended the research for the reasons of the formation of the esters and the search for alternative techniques regarding the processing of refined edible fats and oils with the aim to reduce the content of the esters. Not only the thermal processing such as deodorization and deep-frying can trigger the formation of unpleasant substance such as trans fatty acids cyclic fatty acid esters, but also refining of edible oils, caused to formation of undesirable compounds such as glycidol and MCPD esters. Hence in this research first of all describe MCPD and their esters, then evaluated the situation and different factors which trigger producing this compound and finally give a solution to remove these materials from edible oil.

Table 1. The content of the different contaminants in vegetable oils.

Samples	Contaminants of vegetable oil	References
Pesticides	Rotenone, Simazine, Terbuthylazine, Diuron, Methamidophos Monocrotophos, Omethoate	(Cabras et al., 2002; Cindric et al., 2007; Ramli et al., 2012; Zhao et al., 2013)
Mycotoxins	Aflatoxins B1, Zearalenone, Fumonisins (B1, B2), Deoxynivalenol	(Escobar et al., 2013; Majerus et al., 2009; Siegel et al., 2010)
Heavy metal	Cr, Pb, Ni, Mn, Cu, Co, Al, K, Fe, Zn, Cd, Mo, Ti, V	(Ansari et al., 2008; Ansari et al., 2009; Juranovic et al., 2003)
Polycyclic aromatic hydrocarbons	Naphthalene, Acenaphthylene, Fluorene, Phenanthrene, Pyrene, Benz[a]anthracene, Chrysene, Indeno[1,2,3-cd]pyrene	(Shi et al., 2016)

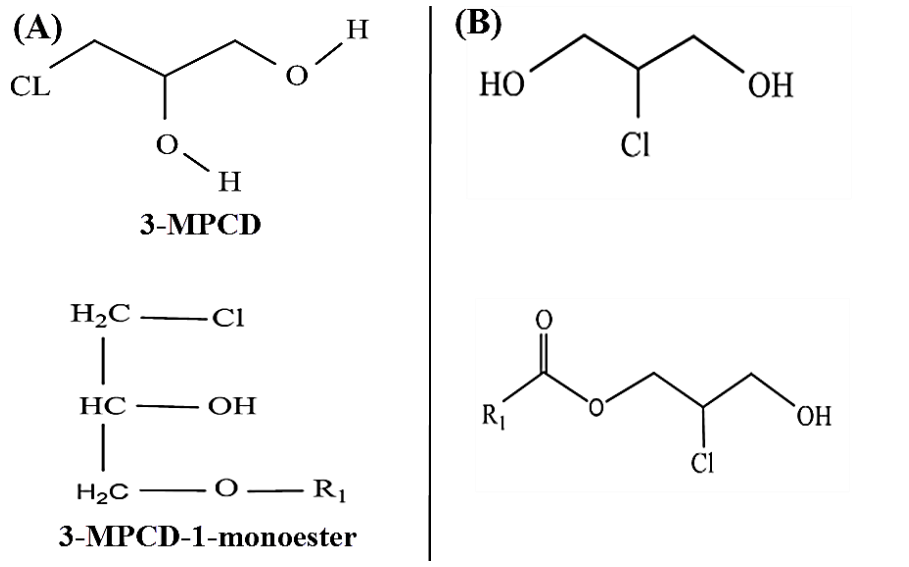

Fig. 1. (A) Structure of 3-MCPD and its monoester; (B) Chemical structure of 2-MCPD and its monoester.

2. Formation of 3-MCPD in vegetables oils

Thermal processing such as deodorization and deep-frying can trigger the formation of unpleasant substance such as trans fatty acids, (Wolff, 1993) cyclic fatty acid esters, (Destaillats et al., 2005) or acylglycerol polymers (Beljaars et al., 1994). During thermal processing at high temperatures, thermo-oxidized products and polymers can be formed. Velisek et al. (1987) reported the formation mechanism of chloropropanols and their esters based on acid hydrolyzed vegetable proteins. Thereafter, chloropropanols and their esters have been detected in vegetable oils as well

(Velisek et al. 1978). Also, chlorination of acylglycerols in deodorization cause to formation of fatty acid esters ofmonochoropropane-1,2-diol (MCPD) and glycidol esters (GE) (Franke et al., 2009; Masukawa et al., 2010; Weißhaar et al., 2010; Zelinkova et al., 2006).In fact, a reaction between triacylglycerols (TAG) and phospholipids cause to MCPD and MCPD esters formation in vegetable oils. From these products 3-MCPD, 1,3-DCP, 2,3-DCP, 2-MCPD have been reported in oilseeds such as soybean and rapeseed (Rahn et al., 2011; Stadler, 2015; Zelinkova et al., 2006).

There are some speculations on the formation mechanisms for 3-MCPD and glycidol in food products (Table 2). Formation of 3-MCPD esters has also been investigated by simulating oil processing under deodorization condition, which proposed that TAG, diacylglycerols (DAG) and monoacylglycerols (MAG) were the precursors of 3-MCPD compounds (Freudenstein et al., 2013).

In some studies, researchers proposed the hypotheses of cyclic acyloxonium ion as a significant factor and key intermediate (Fig. 2). The formation of cyclic acyloxonium ion is based on hydroxylation of diacylglycerols and monoacylglycerols. Finally, 3-MCPD diesters and monoesters have formed by diacylglycerol-derived acyloxonium ion in presence of Cl. It should also be noted that the 3-MCPD monoesters can also be generated by monoacylglycerol-derived acyloxonium ion and GE in presence of Cl (Fig. 2) (Bakhiya et al., 2011; Hamlet et al., 2011).

Table 2. Previously published works on the formation of 3-MCPD.

Researchs	Results	Ref.
Model studies on the formation of monochloropropanediols in the presence of lipase.	Producing 3-MCPD in plant oils and fat with fun gal, plant and mammalian lipase.	(Svejkovska et al., 2006)
Intestinal monoacylglycerol metabolism: developmental and nutritional regulation	2-monoacylglycerol has both catabolic and anabolic procedure in intestinal mucosa.	(Chon et al., 2007)
Esters of 3-chloro-1,2-propanediol (3-MCPD) in vegetable oils: significance in the formation of 3-MCPD	Decomposition of 3-MCPD in an intestinal system by pancreatic lipase and bile extract.	(Seefelder et al., 2008)
Occurrence of 3-MCPD fatty acid esters in human breast milk	The presence of 3-MCPD esters in human breast milk, in fact 3-MCPD fatty acid esters released 3-MCPD, then this ingredient absorb in human	(Zelinkova et al., 2008)
Lipolysis a highly regulated multi-enzyme complex mediates the catabolism of cellular fat stores	Three enzymes have function in hydrolysis of triacylglycerol, including: adipose triglyceride lipase, hormone-sensitive lipase, and monoglyceride lipase.	(Lass et al., 2011)
Absorption and metabolism of the food contaminant 3-chloro-1,2-propanediol (3-MPCD) and its fatty acid esters by human intestinal Caco-2 cells	Caco-2 cells have hydrolyze and metabolize role on the 3-MCPD monoesters and 3-MCPD diesters, respectively.	(Franke et al., 2009)

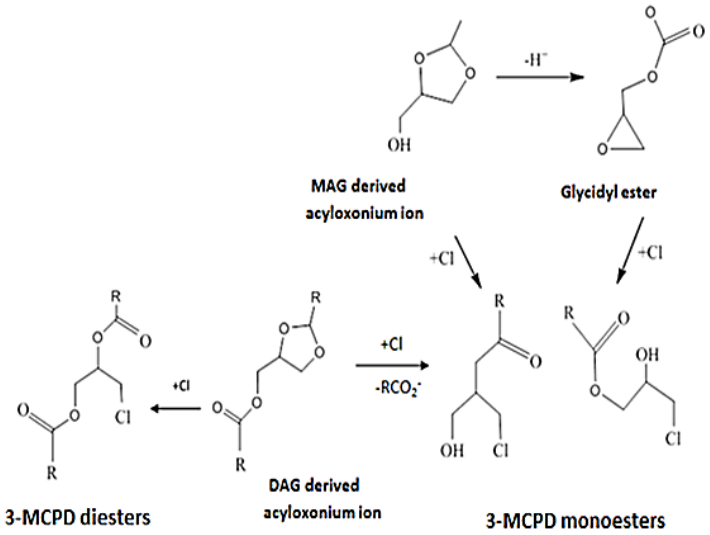

Fig. 2. Procedure of 3-MCPD and glycidol esters from acylglycerols.

Important components of vegetable oils on formation of 3-MCPD during deodorization are free fatty acids, acylglycerols (mono-, di- and tri-), and chloride compounds such as chlorides, hydrogen chloride, otherwise organic chloride composites. Contents of 3-MCPD esters formed during deodorization related to vegetable oils composition. Literature shows that 3-MCPD esters produced from MAG and DAG, TAG or from DAG and TAG (Mathieu Dubois et al., 2012). To minimize the amount of 3-MCPD esters and GE in edible oil, there are some ways, including degumming with reduced acid level based on the crude oil qualities, optimum neutralization prior to deodorization, suitable farming conditions such as using suitable fertilizer, good harvesting condition, removing critical reactants from the raw material, and also changing the refining process and removing formed 3-MCPD esters and GE from refined product (Henderson et al., 2000; Weißhaar, 2008). Although, it is importance to know formation of 3-MCPD from monoesters is faster than diesters during hydrolysis. Monoesters hydrolyses completes in 1 min, but, diesters hydrolyses 45% in 1 min. However, diesters hydrolysis completes after 1 h.

The mechanism of GE formation is through monoacylglycerol-derived acyloxonium ion on the path of producing 3-MCPD (Barocelli et al., 2011; Buhrke et al., 2011; Cheng et al., 2017; Franke et al., 2009; Freudenstein et al., 2013; Liu et al., 2012). Formation of 3-MCPD and GE depend on some conditions including oil component (the amount of free fatty acids, chloride and mono- and diacylglycerides), refining conditions (time and temperature, NaCl content and pH) (Arisseto et al., 2017; Bakhiya et al., 2011; Buhrke et al., 2011).

Another suggested procedure to produce 3-MCPD is an interaction between sodium chloride and free fatty acid which produces hydrogen chloride. Subsequently, the oxygen atom of glycerol oxo group is protonated. Then a 1,3-dioxolan cycle is created with a participation of the hydroxyl group. After water is split off (in the case of monoacylglycerol and diacylglycerol), a cyclic oxonium ion forms. After the nucleophilic substitution by the chloride anion the cycle oxonium (less sterically hindered carbon atom with the ring open) yields either monoester or a 3-MCPD diester. In the same manner, though to a lesser extent, the nucleophilic substitution at the more sterically hindered carbon atom yields monoester or a 2-MCPD diester (Zhang et al., 2015).

Mechanism of *in vivo* formation is based on pancreatic lipases hydrolysis of fatty acids at position 1 and 3 on TAG and production of 1 and 3-monoacylglycerols. This process for TAG is as follow: producing 2-monoacylglycerols, enterocytes absorption, re-esterified and then adding to lipoprotein ingredients. 1-Monoesters could create free 3-MCPD, whereas diesters decompose to 2-monoesters and then absorbed (RJones, 1983). 3-MCPD diester could be changed to 3-MCPD-2-monoacylester and then free 3-MCPD could be formed (Li et al., 2016; Smidrkal et al. 2016).

Palm oil and palm kernel oil are obtained from mesocarp and kernel of the palm fruit, respectively. Crud palm oils are generally physically refined prior to consumption. Main physical refining steps are degumming, bleaching and steam refining (Kyselka et al., 2018). 3-MCPD esters, 2-MCPD and glycidyl fatty acid esters can be produced during steam refining (deodorization) of palm oil at high temperature, (Edem, 1999; King et al., 1984; Manorama et al., 1991) which their content is differ based on the refining condition and palm oil quality (Edem, 1999; Foundation, 1995; Renaud et al., 1995). Chloride values in the range of 4–5 ppm were found in palm oil. A considerable part of this total chlorine in the refined palm oil was rooted from the 3-MCPD-esters. On the other hand, content of diglycerides as the other potential pre-cursor was between 1% and 10% exceeding the 3-MCPD-ester contents by up to five magnitudes (Tiong et al., 2018).

Weißhaar and Perz (2010) have reported that the presence of glycidyl esters in vegetable oils especially palm oil with the highest levels of 3-MCPD.In fact, one of the main source of chlorinate components in palm oil is from plantation and fertilizers (Craft et al., 2012; Strijowski et al., 2011). Good procedure in agriculture and refining can only eliminate partial amount of chlorinate components. Palm oil refining could reduce the amount of different contaminant. Using calcinated zeolite and synthetic magnesium silicate could reduce the amount of GEs in a range of < 40% in palm oil. There are reports on good efficiency of activated carbon on reducing of the contaminants in the vegetable oils as well, for instance GEs could be reduced in palm oil by activated carbon (Cheng et al., 2017).

2.1. Effect of different condition in 3-MCPD formation

2.1.1. Heat treatment and temperature

Heat treatments have enhanced significantly ($p < 0.05$) the amount of 3-MCPD esters in raw and filterable oils with some exception. Thermal treatment of food containing lipids, certain amino acids, and sugars processed at temperatures above 160 °C may lead to the formation of many toxic compounds such as acrylamide, furan, and a new born class of thermal processing contaminants 3-monochloropropane-1,2-diol (3-MCPD) and its fatty acid esters. The levels of the compounds increase exponentially with temperature up to the maximum (about 220 °C). The range of 3-MCPD esters in filterable oils is between 144.4 to 2321.7 mg/kg. In fact, the amount of 3-MCPD raised in filterable oils with heat treatment. The highest amount related to rape seed oil with 2568.6 mg/kg followed by camellia oil, with 1879.2 mg/kg and peanut oil with 1716.8 mg/kg. The reason for this difference was not clear (Pope et al., 1966; Van Duuren et al., 1974; Weißhaar et al., 2010). Heating have important role information of 3-MCPD.The amount of 3-MCPD increased sharply at the range of 160 to 220 °C, but in the lower than 160 °C there were not significant differences ($p > 0.05$). 3-MCPD reached to the highest amount (10000 µg/kg) at 220 °C and then decreased. These changes related to the formation and decomposition of 3-MCPD during processes. The formation rate was more than the degradation rate at the ranges between 220 to 250 °C. However this condition is vice versa and consequently the amount of 3-MCPD have decreased at 250 °C (Freudenstein et al., 2013; Smidrkal et al., 2011).

In addition, frying duration, frying temperature and NaCl have considerable impact in formation of 3-MCPD esters and glycidyl fatty acid esters. The amount of 3-MCPD ester has direct correlation with frying temperature and concentration of NaCl, but 3-MCPD esters trend was decreased when the frying duration increased. This trend for GEs increased by enhancing of frying temperature, frying duration and concentration of NaCl (Wong et al., 2017).

2.1.2. NaCl and pH

Direct and indirect correlations between NaCl and pH with 3-MCPD esters formation have been approved. One reason for direct relation between 3-MCPD and NaCl is related to Cl ion in NaCl. Also, there was no significant change in the formation of 3-MCPD

in concentration more than 132 g/L Cl because of the saturation of NaCl mixture (Wong et al., 2017).

There was a highest value of 3-MCPD (4000 µg/kg) at pH 3.0 and the lowest amount of 3-MCPD have been observed to pH 7.0 (almost 66 µg/kg). Therefore, 3-MCPD content was promoted by the acidic condition. In comparison between NaCl and pH conditions, the level of ionization for chloride by NaCl is more effective than the acidic pH (Cho et al., 2008).

Table 3. previously published works on the extraction of 3-MCPD.

Matrix	Analytes	Technique	Sample preparation	LOD/LOQ	Ref.
Various	3-MCPD	GC/MS	Extraction with hexane sample mix with pure water and IS, shake for 3h, stand overnight GC/MS, add Nacl for extraction on Extrelut elution with ethyl acetate concentration derivatisation with p-TsOH* monohydrate in dry acetone at 40°C for 90 min	LOD < 5 µg kg^{-1}	(Meierhans et al., 1998; Retho et al., 2005)
Soy sauce	3-MCPD	GC/MS	Similar to AOAC/EN method Derivatisation with 4-heptanone + p-TsOH* in ether at 100°C for 90 min	LOD: 0.48 ng g^{-1}/ LOQ : 1.2 ng g^{-1}	(Leon et al., 2008)
Soy sauce	3-MCPD	CE/ED	Dilution of sample in running buffer Filter	LOD 0.13 µg mL^{-1}	(Huang et al., 2005; León et al., 2008)
Various	3-MCPD & 1,3-DCP	PTV-LVI/GC/MS-MS	Several cleaning and drying steps Similar to AOAC/EN method (above); difference is the large volume injection (LVI)	3-MCPD LOD: 0,0044 ng. mL^{-1}	(Jeong et al., 2010; León et al., 2008)
Soy sauce/HVP aqueous sample	3-MCPD & 1,3 DCP	HS-(SPME)/ GC/MS	Extraction via headspace, but rest of sample preparation varies between the three	LOD: < 4.62 ng ml^{-1}or < 5 µg kg^{-1}	(Crews et al., 2002; Huang et al., 2005; Lee et al., 2007)
Seasoning and Foodstuff	3-MCPD	GC/MS	Sample mix with water add NaOH to pH 8.5 extraction on extrelut elution with ethyl acetate add IS concentration	3-MCPD LOD: 0.1 mg kg^{-1}	(Wittmann, 1991)
Edible oil, Fish oil and Margarine	3-MCPD & 2-MCPD	GC/MS	SGS "3-in-1"	3-MCPD and 2-MCPD LOD: 0.01 mg kg^{-1} / LOQ: 0.03 mg kg^{-1}s	(Jedrkiewicz et al., 2016)
Edible vegetable oils	3-MCPD	UHPLC-MS/MS	Matrix solid phase dispersion extraction	LOD: 0.0001–0.02 mg kg^{-1} LOQ: 0.0004–0.05 mg kg^{-1},	(Li et al., 2015)

3. Analysis of 3-MCPD

3.1. Extraction techniques

Some important methods were used for determination of 3-MCPDesters summarized in Table 3. 3-MCPD esters have a simple chemical structure, however, these esters can be converted to free 3- MCPD which is inflexible to analyze, because of properties such as, low molecular weight, high boiling point and lack of an appropriate chromophore. The lack of an appropriate chromophore affects detection of free 3-MCPD. Therefore, there is a need to high-performance liquid chromatography (HPLC) with fluorescence or ultraviolet (Hu et al., 2013).

High boiling point and low molecular weight of 3-MCPD esters make some difficulties in analyses by gas chromatography-mass spectrometry (GC-MS). Free3-MCPD is derivatized because of high polarity and low volatility. Derivatisation makes it possible to direct analysis by GC without adverse reactions with matrix or GC system. Also, low molecular weight of 3- MCPD esters affects their detection by mass spectrometry. This factor makes it difficult to diagnose 3-MCPD esters from the background noise. Therefore, analysis of these compounds requires complex sample preparations and derivations. Recently, determination of these compound at levels of ng/g by methods based on solid phase extraction (SPE), derivatisation and subsequent analysis by GC-MS has become possible (Hamlet et al., 2002; Racamonde et al., 2011; Retho et al., 2005; Schlatter et al., 2002; Wenzl et al., 2007).

In lipid samples, the extraction methods which have been used for 3-MCPD esters classified in tow groups, direct and indirect analytical approaches (Renata Jedrkiewicz et al., 2017; Zelinkova et al., 2017). Direct procedures evaluated monoesters and diesters by liquid chromatography-mass spectrometry, such as LC-MS/MS and LC-TOF-MS (MacMahon et al., 2013; Yamazaki et al., 2013; Zelinkova et al., 2009). It needs sample extraction, clean-up by SPE and final quantification by liquid chromatography-mass spectrometry. Nevertheless, it did not get application in routine

analysis, due to needs of analytical standards and challenging separation (Pope et al., 1966).

Indirect approaches were applied for determination of 3-MCPD esters in lipid samples in most cases. These methods are based on acidic and alkaline transesterification reaction with releasing free chloropropanediol by liquid-liquid extraction (purification), derivatisation and quantification by GC-MS. However, this method has multi-step sample preparation procedure which may have side reactions. This method usually used in quality control research laboratory, because of some properties such as simplicity, fastidiousness and cheapness in case of chromatographic separation (Van Duuren et al., 1974). One of the critical stages in indirect methods is conversion of 3-MCPD into glycidol by transesterification reaction especially in an alkaline environment. A great solution to come across with the problem is reducing pH or conducting transesterification reaction in acidic environments (Ermacora et al., 2013).

4. Toxicological effects

4.1. 3-MCPD

Recently, the carcinogen effects of free 3-MCPD and its fatty acid have been evaluated in some products such as coffee, edible oils, infant formula (Dubois et al., 2018; Leigh et al., 2017), potato based products, bakery products, malt, cooked meat, soy sauces and pickles (Hamlet et al., 2002; Pudel et al., 2011; Svejkovska et al., 2004; Weißhaar et al., 2010).Researchers could also detect esters of 3-MCPD in human breast milk in a concentration between 6 to 76 lg/kg milk. 3-MCPD was also detected in human organs (Zelinkova et al., 2008; Zelinkova et al., 2006).

The assumption of toxicological 3-MCPD and glycidol esters are based on releasing free 3-MCPD or glycidol from 3-MCPD esters by lipase-catalyzed hydrolysis during digestion in the gastrointestinal tract (Buhrke et al., 2011; Zelinkova et al., 2008). The JECFA, (JECFA, 2016) announced a regulatory maximum TDI of 2 µg/kg body weight (bw) per day for free 3-MCPD and 3-MCPD esters. Meanwhile, the EFSA (Chain, 2016) established a tolerable daily intake (TDI) of 0.8 µg/kg bw per day for the sum of free 3-MCPD and 3- MCPD esters.

Weight which established by European Commission's Scientific Committee on Food in 2001 (JECFA, 2016) and known as an non-genotoxic carcinogen (Bakhiya et al., 2011). The toxicity, carcinogenicity and mutagenicity of 3-MCPD have also been studied by the joint FAO/WHO expert committee on food additives (Beekman et al., 2018; Organization, 2016).

Carcinogenic effects of 3-MCPD have two aspects in short term and long term. 3-MCPD have negative impact on kidney in rat and mice in short term and cause to acute glomerular nephritis, and proteinuria and glucosuria in male rat (Jones et al., 1978; Morris et al., 1980). Also, the effect of 3-MCPD on bone marrow in primate has been assessed. In long term study, researcher have examined subcutaneous and the intra-peritoneal issue in Swiss rats, (Van Duuren et al., 1974) SD rats, (Cho et al., 2008; Weisburger et al., 1981) Fischer 344 rats, (Cho et al., 2008; Sunahara et al., 1993) B6C3F1 rat (Jeong et al., 2010) and finally confirmed the carcinogenicity properties in rats (Cho et al., 2008; Jeong et al., 2010).The results of mutagenicity by 3-MCPD was positive in vitro, in lymphoma cells Tk and V79 cells (Henderson et al., 1987; May 1991; Ozcagli et al., 2016; Zeiger et al., 1992).One of the considerable effects of 3-MCPD mutagenic properties is dechlorination of 3-MCPD and producing glycidol in Salmonella typhimurium (Zeiger et al., 1992).

Toxicological properties of 3-MCPD and 3-MCPD di-palmitic esters in male and female rats have been evaluated and equimolar dosage of free 3-MCPD was 30% higher than of di-palmitic esters in urinary metabolites,(Barocelli et al., 2011) which showed significant bioavailability of 3-MCPD. Finally, it was confirmed that, kidney and testes in male rat are vulnerable tissues to 3-MCPD and 3-MCPD di-palmitic esters (Barocelli et al., 2011; Yan et al., 2018).3-MCPD caused infertility in male mice, (Jones et al., 1978) in a dose more than daily intake (2 µg/kg body weight per day), and about other species for instance, hamsters, rams, monkey and dogs at dose more than 20 mg/kg body weight (bw) per day. In fact, these components declined action of sperm and had negative effects in fertility (Irwin et al., 1996; Jones et al., 1978; Kwack et al., 2004).

Refining of edible oils, although eliminates contaminants from the oil, but it leads to formation of unwanted compounds such as glycidol, glycidol esters, MCPD and MCPD esters. Zelinkova et al. (2006, 2009) have discovered small amount of free MCPD in physically refined vegetable oils. It should be mentioned that large amount of MCPD can be produced by using of acid methanolysis method and chloride (Weißhaar et al., 2010). Also, bound glycidol esters are produced in a way similar to MCPD (Smidrkal et al., 2011; Zelinkova et al., 2006). Glycidyl esters may release glycidol, which has a greater carcinogenic effect in animals (Weißhaar et al., 2010).

Glycidol have mutagenic and carcinogenic properties in animals but there were no realistic data on human by now. One of the examples about the carcinogenic effect of glycidol related to B6C3F1 and F344/N rats in 16 days of experiment. All of the animals which have received 600 mg/kg bw per day, died on fourth day of experiment. One of the strongest hypothesis about this issue was acute injury in the medulla and thalamus (Irwin et al., 1996). In another research,344 rats and B6C3F1 mice (both sexes) selected and the survival of animals have been evaluated in water feed with glycidol at the different dose of glycidol for rats and mice, 0, 0.37, 75 mg/kg bw per day and 0, 25 ,50 mg/kg bw per day, respectively. The result of this study showed that the most sensitive organs to glycidol were harderian gland in both sexes in mice, fore stomach in males' mice, and the mammary gland in females' mice. However, there were no negative effect on kidney (Irwin et al., 1996).

5. Conclusion

Vegetable oils are the main part of our diet. Taking into account the hazardous properties of MCPD and related compounds and their presence in the vegetable oils, it is important to have knowledge on these compounds to minimize their health implications. The refined oils had higher level of 3-MCPD esters than the crude oils. The formation of the 3-MCPD esters is found to be affected not only by high temperatures, but also by acidity during the refining process. The formation of 3-MCPD esters can be limited by manipulating above influential factors during the manufacturing of oils or family cooking. There is valuable information on the MCPD and the related compounds formation and analysis; however, there are need to more researches on some gaps in their formation routs and also simplification of the analytical methods.

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