Available online at www.derpharmachemica.com

ISSN 0975-413X
CODEN (USA): PCHHAX

Der Pharma Chemica, 2017, 9(7):84-90
(http://www.derpharmachemica.com/archive.html)

Review on 3-Chloro-1,2-Propanediol: A Chloropropanol Formed During Food Processing

Belay Haile, Neela Satheesh*

Department of Postharvest Management, College of Agriculture and Veterinary Medicine, Jimma UniversityJimma, Ethiopia

ABSTRACT

Due to the different processing methods in food preparation, leads to the formation of some by-products which are very importance in human health. Chloropropanols are the chlorine containing alcohols determined in different oils and fats related communities in their ester forms. 3-monochloropropan-1, 2-diol (3-MCPD) is one of the major chloropropanols identified in most of the food samples, including vegetables, fruits, eggs and dairy products in very lower limits. Chloropropanols present in foods for number of reasons. Condiments such as soya sauce and oyster sauce, after going through an acid treatment, reported the presence of 3-MCPD. Other ready to eat food products, like instant noodles and hamburgers, used acid-hydrolysed vegetable protein as an ingredient, also reported the evidence of 3-MCPD. Lipids and sodium chloride in foods also contribute to the formation of 3-MCPD during normal heat processing such as coffee roasting and bread-baking. Researchers have been proved genotoxic effect of 3-MCPD and still research is going on the health effects of chloropropanols. In present review we are presenting the introduction, occurrence in different types of the food materials, dietary exposure and their biotransfermation, toxicity of 3-MCPD. Also, presented the direct and indirect detection methods and presented with potential solution for degradation of Chloropropanols in different food products.

Keywords: Chloropropanols, Oil, Food stuffs, Domestic cooking, Genotoxic

INTRODUCTION

Chloropropanols are chlorine containing C3 alcohols have been found as growing significance to the fats and oils community, particularly in their esterified (or bound) state. The chloropropanol most commonly found in food, in either its free or bound form, are 3-MCPD (3-monochloropropane-1,2-diol), although others are also of interest, including 2-MCPD (2-monochloropropane-1,3-diol), 1,3-DCP (1,3-dichloro-2-propanol), and 2,3-DCP (2,3-dichloro-1-propanol) [1-3].

It was reported that; 3-MCPD and 1, 3-DCP are primary members of chloropropanols found in food, in either it's free or bound (esterified) form. However, 3-MCPD is usually found in higher concentrations than 1,3-DCP in food with edible oils (especially refined oils) represent the main source of these contaminants in thermally processed foods [4-6]. Structures of common chloropropanols are showed in Figure 1 [7].

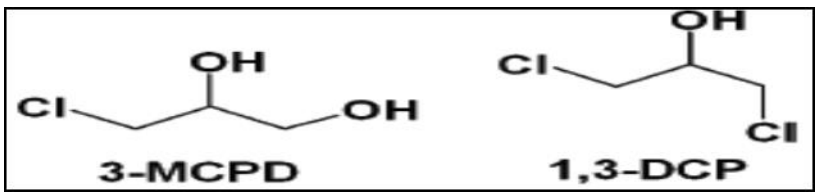


Figure 1: Chemical structure of the two most common chloropropanols

MATERIALS AND METHODS

3-MCPD is a colorless liquid but has a tendency to turn straw-yellow and is soluble in water, alcohol, diethyl ether, and acetone. Industrially, it has been used to lower the freezing point of dynamite, as a dye intermediate, as a rodent chemosterilants, and as a solvent for cellulose acetate [7]. In the food industry, 3-MCPD is a by-product of acid-hydrolyzed vegetable protein (acid-HVP) production [7]. 3-MCPD; was detected in acid-Hydrolysed Vegetable Protein (HVP) [8], various heat-processed foods, food ingredients and coffee beans [9-13].

Now-a-days great attention has been paid by researchers to 3-MCPD and the related substance. Dietary exposure to 3-MCPD can affect male fertility, kidney functioning, and body weight of rats when regularly ingested in large amounts [14,15]. Available toxicity results have shown that 1, 3-DCP is a genotoxic, hepatotoxic, and cancer-inducing agent, and it has been classified as being possibly carcinogenic to humans [7].

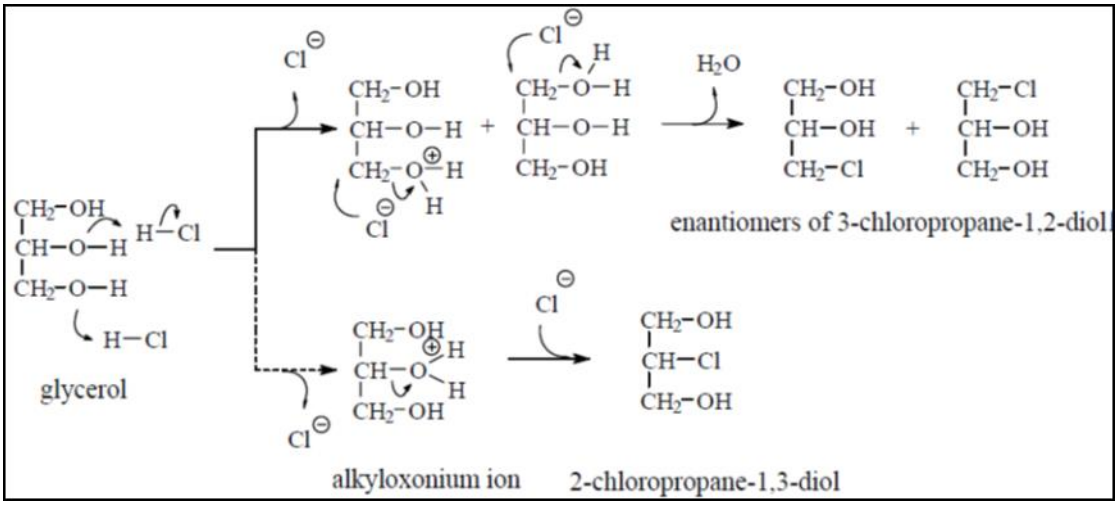
The main objective of this paper includes reviewing the resent research related to the 3-MCPD and their potential health effects with the elimination methods.

Occurrence

3-Monochloropropane-1,2-dio l (3-MCPD) is a contaminant belongs to a group of chemicals called chloropropanols; was first identified as a contaminant of soy sauce and Acid-hydrolysed Vegetable Protein (HVP), which is a flavouring agent in soy sauce production [8]. The acid-HVP is a process used to mass-produce artificial soy sauce in a short period of time, without the fermentation process [7] and confirmed later in edible oils and fats [16-25] as well as in oil-based foodstuffs [26].

Although, it has been detected in a number of food groups such as meat, dairy, cereal, soup and miscellaneous products [27-29], food ingredients like malt products (brewing malts, malt extracts, malt flours), breadcrumbs, enzyme HVPs, meat extracts, modified starches [9], soy sauces and similar products [11,12,30-34], coffee [13], coffee surrogates [35] infant and baby foods [36], potato products [37].

3-MCPD is characteristic of a variety of processed foods; occurs in many foodstuffs in its free form and also in the form of esters with higher fatty acids. It is formed mainly when fat-containing foods that also contain salt are exposed to high temperatures i.e., reaction between lipid components (glycerol or glycero-lipids) with salt (chloride ions). The reaction proceeds either via direct nucleophilic substitution of acyl and/or hydroxyl groups by chloride ions, or by opening the cyclic acyloxonium ion intermediates of diacylglycerols with chloride ions to form diesters and monoesters of 3-MCPD in acid-HVP as showed in Scheme 1 [4-6,8,38].



Scheme 1: Reaction of HCl with glycerol

Fatty acid esters of 3-MCPD (monoesters and diesters with higher fatty acids) were the known precursors in the formation of free 3-MCPD (Figure 2) associated with food processing procedures using hydrolysis with hydrochloric acid [38].

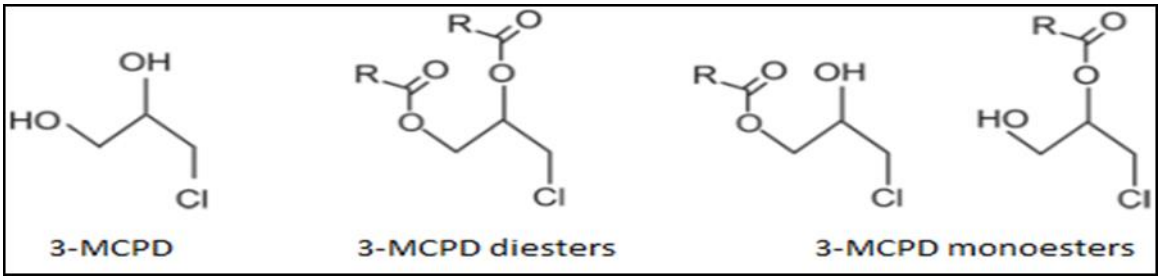


Figure 2: Fatty acid esters of 3-MCPD (R=alkyl)

The application of mass defect-based filtering approach used to describe the source of halogenated contaminants and their precursors in edible oils to generate a hypothesis on the identity and occurrence of those thermally labile, chlorinated contaminant precursors that may act as chlorine donors during the formation of MCPD esters.

In-vitro experiments confirmed that the level of organochlorines present in palm oil decreased progressively upon heat treatment, while the level of MCPD esters increased. Consequently, it is postulated that during oil refining these organochlorines naturally present in palm fruits act as a 'chlorine source' for the generation of MCPD diesters [39].

The levels of 3-MCPD formed in food by the interaction between chloride ions and lipids depends on temperature, water, fat and salt contents of systems simulating processed foods. The reaction of 3-MCPD precursors (i.e., glycerol, triolein, lecithin) with sodium chloride in an emulsion stabilised with an emulsifier under conditions which modelled the thermal treatment of foods during processing yielded two enantiomers of 3-MCPD, i.e., (R)-3-MCPD and (S)-3-MCPD as a racemic mixture (Figure 3) [3,40,41]. The two enantiomers are found in equimolar concentrations in protein hydrolysates produced by hydrochloric acid hydrolysis [42].

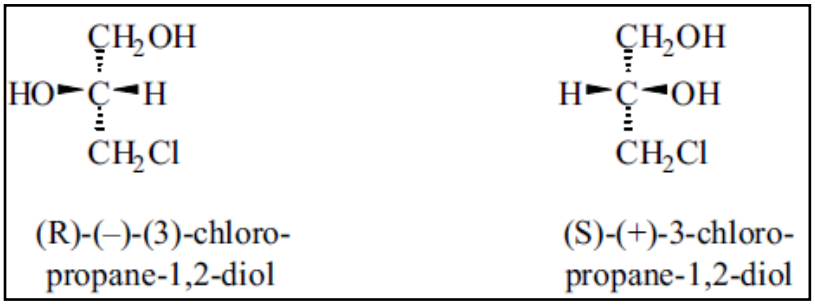


Figure 3: Streoformulae of optically active 3-chloropropane-1, 2-diols

Dietary exposure

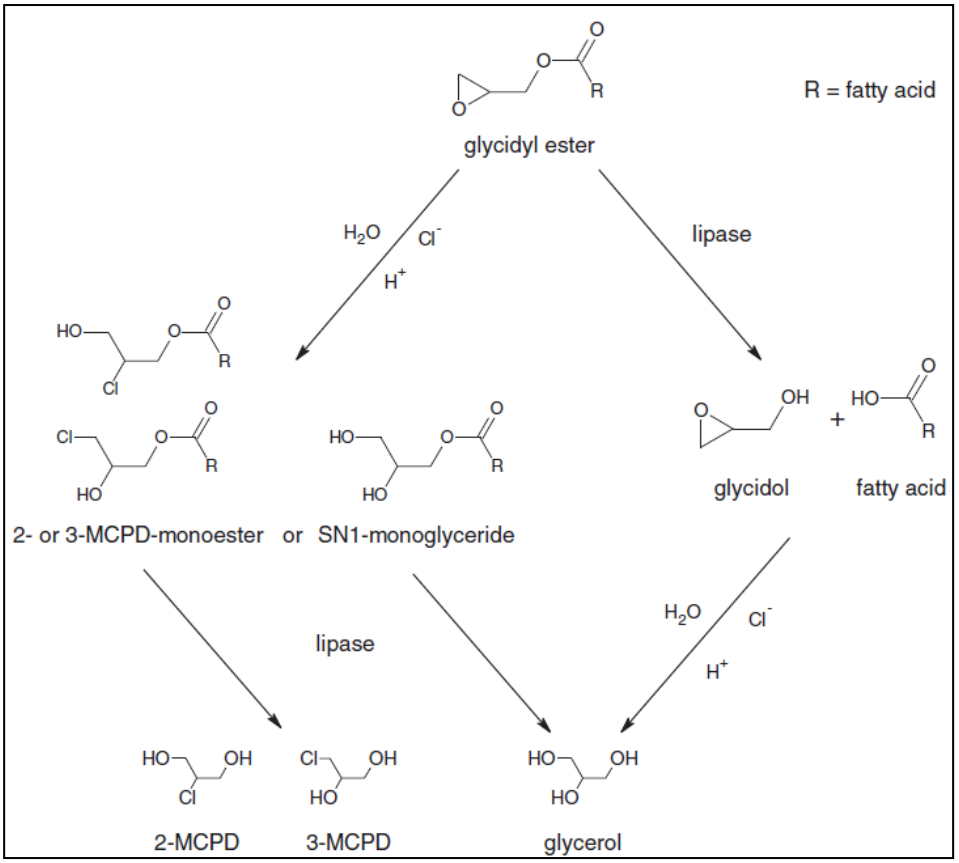
Chronic dietary exposure data dictates that the highest amount of 3-MCPD esters was determined in samples of edible oils and fats destined to household consumption [23,43]. *In-vitro* experiments confirmed that in oil refining process 3-MCPD esters can be produced at the deodorization step [44]. This phenomenon coincided with the decomposition of organochlorines present in the oil, as well as the formation of MCPD diesters at high temperatures. The mechanism involves the reaction of Triacylglycerols (TAG) with a reactive chlorinated molecule (e.g. HCl) that evolves through the decomposition of naturally occurring chlorinated constituents of the oil and results in the formation of MCPD diesters [5,9,39].

Domestic cooking procedures, including toasting, microwaving and grilling, have been shown to produce elevated 3-MCPD levels in some foods and especially in toasts [27]. Although, several studies have shown that elevated levels of 3-MCPD can also occur in a wide range of foods and food ingredients (e.g. in bakery products, cakes, meat, dairy products and malt) formulated without acid-HVP as a result of processing. The concentration in toast increases proportionally to the degree of browning and whole meal content. Likewise, the smoking of meat products is a possibility to form 3-MCPD. The content depends on the smoking technique, the used firewood and the duration within the smoking chamber. 3-MCPD has also been found in liquid flavour. During barbecuing, it may develop as fat drips on glowing charcoal [10-12,45].

Certain types of fermented sausage such as salami have also been shown to contain 3-MCPD. This may be due to the formation of 3-MCPD within the meat (due to the interaction between fat and salt in the product, coupled with its long shelf life) and/or due to the presence of 3-MCPD in the resins used in the sausage casings. Most acid-HVP is produced using hydrochloric acid. 3-MCPD is formed as a result of the high temperature chlorination of lipids present in the protein starting materials, 1,3-DCP can then be formed from the 3-MCPD precursor [8-13].

Biotransformation

It was proposed that the presence of Glycidol Esters (GEs); Fatty acid esters of glycidol (3-hydroxy-1, 2-epoxypropane) could be the source of significant overestimation of 3-MCPD esters. Because of their structural similarities with triglycerides and MCPD esters, GEs are anticipated to be hydrolysed in the gastrointestinal tract through the action of lipases, potentially releasing an epoxide known glycidol. Due to the presumed instability of the epoxide group under stomach conditions, a ring-opening and chlorination could be expected leading potentially to the formation of 2-MCPD or 3-MCPD monoesters, depending on the position of the carbon at which nucleophilic attack took place when the nucleophile is chlorine (Scheme 2) showed in Figure 4 [19,22,42,46-48].



Scheme 2: Hypotheses of possible degradation pathways illustrated for glycidyl esters

3-MCPD esters are suitable substrates for intestinal lipases due to their structural similarities with acylglycerols. If 3-MCPD esters present in food it may release a certain amount of 3-MCPD by action of intestinal lipases, contributing to the overall dietary exposure to 3-MCPD. Although both the 3-MCPD-1 monoesters and the 3-MCPD diesters are accepted as substrates by intestinal lipase, the hydrolysis of 3-MCPD esters is unlikely to release 3-MCPD fully. The well-known preference of intestinal lipases for position sn-1 and sn-3 of acylglycerols explains the more efficient release of 3-MCPD from the sn-1-monoesters than from the diesters. Indeed, triglycerides are hydrolysed *in vivo* to 2-monoglycerides and subsequently absorbed by the mucosa. Hence, the relative concentrations of mono- and diesters are expected to have a significant impact on the intestinal release of 3-MCPD *in vivo* [19,48].

3-MCPD-1-monoesters may simply be considered as additional free 3-MCPD, because these monoesters are quickly hydrolysed, thereby releasing free 3-MCPD. In case of 3-MCPD diesters, there are two possible mechanisms of metabolism. One of them is luminal hydrolysis by pancreatic lipase leading to an increase in the burden of free 3-MCPD, whereas the second one is possible mechanism intracellular metabolism by intestinal cells would not lead to increased amounts of the free substance. Therefore, it needs further study to identify which of the two possible mechanisms is favored under *in vivo* conditions [49].

Toxicity

Ingestion of free 3-MCPD is neither absorbed nor metabolised by the human intestinal cells, but migrate through cell monolayer barrier to induces various adverse effects on the kidney and on the reproductive systems of the mature male rat based on the increased incidences of kidney renal tubule carcinomas and Leydig cell tumors [47,50]. 3-MCPD induced morphological changes and DNA damage of Leydig cells result in early apoptotic cell death [15].

Leydig cells are the primary source of testosterone in males and their differentiation in the testes is an important event in the reproductive system development of male. Steroid hormone synthesis is initiated with the Steroidogenic Acute Regulatory (StAR) protein, a key factor in the transfer of cholesterol from the cytoplasm into the inner membrane of mitochondria. In the mitochondrial inner membrane, cholesterol is converted to pregnenolone by cytochrome P450 side-chain cleavage enzyme (P450scc). Pregnenolone is then transported to the smooth endoplasmic reticulum and sequentially converted into progesterone by 3β-hydroxysteroid dehydrogenase (3β-HSD) [15].

The Scientific Panel on Contaminants in the Food Chain; former European Commission's (EC) Scientific Committee on Food and the Joint FAO/WHO Expert Committee on Food Additives (JECFA) set a tolerable daily intake (TDI) of 2 µg/kg of body weight in 2001.

(The TDI is an estimate of the amount of a substance in air, food, or drinking water that can be taken in daily over a lifetime without appreciable health risk.) In 2008, JECFA set the maximum allowable content of free 3-MCPD in foods at 0.4 mg/kg (400 μg/kg) for liquid condiments [2,14,19].

Determination

Determination of chloropropanols includes aqueous extraction, matrix spiking of a deuterated surrogate internal standard (3-MCPD-d_5), clean-up using Extrelut^{TM} solid-phase extraction, derivatisation using a silylation reagent, and GC-MS analysis of the chloropropanols as their corresponding trimethyl silyl ethers [31,51].

The proposed analytical approaches for determining 3-MCPD esters involve both indirect analysis, in which the total concentration of the compounds is measured as free 3-MCPD obtained after a hydrolysis/transesterification procedure, and direct analysis, in which the different species of 3-MCPD esters are individually identified. The transesterification included methanolysis catalysed by acidic or alkaline conditions, and hydrolysis by lipase prior to derivatisation and quantification [21,23].

Direct method

A direct analysis method, using HPLC–time of flight mass spectrometry (LC–TOFMS) not required any harsh chemicals prior to analysis and had adequate detection limits for MCPDE and glycidol ester (GE) in the samples. However, both the acid and the base transesterification procedures use hazardous chemicals which may alter MCPD concentration. Acid catalyzes the formation of MCPD from chloride and, even though sulfuric acid is used, chloride in the samples could result in synthesis of MCPD during the treatments. Sodium methoxide also has problems in that base catalyzed reactions can degrade MCPD, as it is not to be stable above pH 6.0 [52].

Liquid Chromatography-tandem Mass Spectrometry (LC-MS/MS) has been used to quantify 3-MCPD esters directly in edible oils from soybean, rapeseed, rice, safflower, sesame, olive, grape seed, perilla and palm. HPLC separation is performed using a reversed phase column and mass data from MS is obtained using Electro Spray Ionization (ESI) operated in positive mode [21].

Indirect method

Since there is no suitable chromophore in their structures, approaches based on HPLC are not applicable. Also, the low volatility of chloropropanols, especially 3-MCPD and 1, 3-DCP, makes direct analysis by GC-MS difficult. Moreover, the low molecular weight of chloropropanols causes problems in distinguishing the MS target ions from background noise. These limitations have been overcome by derivatisation methods required to produce more volatile analytes and prevent the undesired interaction of chloropropanols with other components during preparation and GC analysis [51].

Direct methods of analysis offer the major advantage of providing information on the ester composition, but at the same time, their major drawbacks are associated with the quantification of a large number of individual species. Indirect methods seem to be better suited for routine analysis because of their higher sensitivity and the need of just a single standard for the quantification [53].

Indirect methods of 3-MCPD esters analysis are based on a common series of steps that include the acid- or alkaline catalyzed cleavage of the esters to yield the free form, followed by the purification of the analyte from the fatty acid methyl esters formed during the methanolysis, derivatization of the free 3-MCPD (using either Phenyl Boronic Acid (PBA), hepta fluorobutyrylimidazol (HFBI) and acetone) followed by injection of the derivatized sample in GC–MS [20,26].

The derivatisation step, which is a crucial step in chloropropanols analysis, is intended to give more reliable MS characteristic ions due to increased molecular weight, formation of volatile and stable 3-MCPD derivatives that may be readily characterized by selective MS detection [35]. So, in derivatization step, concentrated extracts of 3-MCPD reacted with HFBI, PBA and acetone to give the corresponding diester of 3-MCPD, non-polar cyclic derivatives extractable into hexane and substituted 1,3-dioxolane respectively (Figure 5) [20,23,35,45].

However, a qualitative and quantitative determination method for chloropropanols in soy sauce by GC-MS/ MS with coupled column separation without derivatisation was developed by Xu et al. Comparing the normal GC-MS method with derivatisation, the method developed in this study was simple, sensitive and reduced solvent consumption. Also, it was effective in suppressing matrix interferences. The coupled column had the properties of giving less column bleeding and improved peak tailing for chloropropanols without chemical modification. Furthermore, the short coupled polar column can also prevent the followed main analysis column from contamination with high molecular weight matrix substances [33].

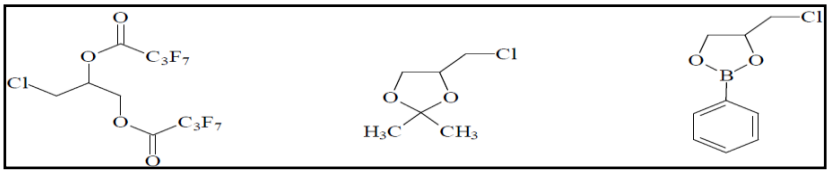


Figure 5: Reaction products of 3-MCPD with derivatisation reagents: (a) heptafluorobutyryl imidazole; (b) acetone; (c) phenylboronic acid

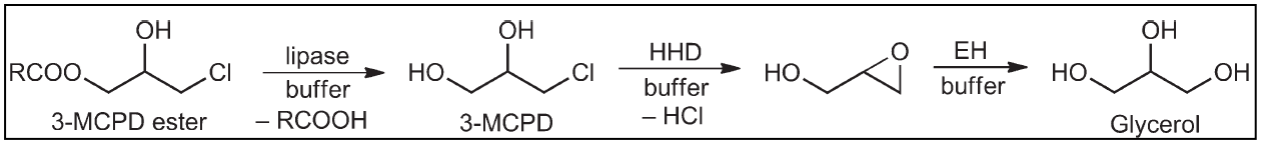
Reduction of 3-MCPD

As mentioned earlier, glycidol esters; fatty acid esters of glycidol could be the possible source of significant 3-MCPD esters the known precursors in the formation of 3-MCPD. Both 3-MCPD esters and glycidyl esters are formed during the deodorization step of the edible oil refining process due to the effect of high temperature. But, the level of 3-MCPD esters seems to be independent of the refining conditions and is primarily determined by the oil type. On the other hand, the levels of formation of glycidyl esters were shown to be affected by the parameters of the deodorization process [19,20,54].

The results suggest that the mitigation of glycidyl ester formation through optimized refining may be more promising than the mitigation of 3-MCPD ester formation. Limiting the level of glycidyl esters formed during deodorization by decreasing the deodorization temperature (or the residence time) may be feasible assuming the operation can be optimized in such a way that other contaminants and FFAs are sufficiently removed from the oil [20].

Comprehensive studies have been undertaken to mitigate the formation of ME and glycidyl esters (GE esters). The mitigation procedures can be generally divided into three approaches: removal of precursors in the raw material, modification of the refining process and removal of the esters post refining [55].

Enzymatic approach can be used for the detoxification of edible oils for nutrition from 3-MCPD contamination. The basic concept for the enzymatic removal of 3-MCPD and its fatty acid esters is shown in Scheme 3 [56]. A 3-MCPD fatty acid ester is first hydrolyzed by a lipase to furnish the free 3-MCPD followed by subsequent enzymatic conversion to glycerol. Then free 3-MCPD is converted to the corresponding epoxide glycidol by Halohydrin Dehalogenase (HHD), which is finally hydrolyzed by an epoxide hydrolase (EH) to glycerol. Therefore, the combination of an HHD and an EH EchA enables the easy removal of the food contaminant 3-MCPD to the nontoxic product glycerol via glycidol [56].



Scheme 3: Enzymatic degradation of 3-MCPD and its fatty acid ester

CONCLUSION

3-MCPD is the most principal chloropropanol, which become a significant contaminant of fats and oils. Since it is formed in thermal processing of foods especially during domestic cooking procedures, includes toasting, microwaving and grilling, and toasting. In edible oil refining process; deodorization step is the most responsible for the formation of 3-MCPD. There are two possible determination methods i.e., direct method (no derivitatiozation) and indirect methods (long steps in sample preparation).

The detoxification of edible oils from 3-MCPD contamination can be assured by enzymatic approach which employs hydrolysis of 3-MCPD fatty acid ester by a lipase to furnish the free 3-MCPD followed by subsequent enzymatic conversion to glycerol which is nontoxic.

ACKNOWLEDGEMENTS

Both the authors are highly thankful to the Department of Post-Harvest Management and College of Agriculture and Veterinary Medicine, Jimma University, Jimma, Ethiopia to providing the facilities to make this review.

REFERENCES

[1] P. Collier, D. Cromie, A. Davies, *J. Am. Oil. Chem. Soc.*, **1991**, 68, 785.
[2] C. Watkins, *Inform Magazine of the AOCS*, **2009**, 4, 52.
[3] J. Velisek, P. Calta, C. Crews, S. Hasnip, M. Dolezal, *Czech. J. Food. Sci.*, **2003**, 21, 153.

[4] B. Svejkovska, O. Novotny, V. Divinova, Z. Reblova, M. Dolezal, J. Velisek, *Czech J. Food. Sci.,* **2004**, 22, 190.
[5] S. Mac Mahon, T.H. Begley, G.W. Diachenko, *Food. Addit. Contam.: Part A.,* **2013**, 30, 2081.
[6] S. Chung, B.T. Chan, H. Chung, Y. Xiao, Y. Ho, *Food. Addit. Contam.: Part A.,* **2013**, 30, 1248.
[7] B. Lee, S. Khor, *Comp. Rev. Food. Sci. Food. Saf.,* **2015**, 14, 48.
[8] J. Velíšek, J. Davidek, J. Hajšlová, V. Kubelka, G. Janíček, B. Mánková, *Zeitschrift für Lebensmittel-Untersuchung und Forschung,* **1978**, 167, 241.
[9] C. Hamlet, S. Jayaratne, W. Matthews, *Food. Addit. Contam.,* **2002**, 19, 15-21.
[10] C. Crews, P. Hough, P. Brereton, D. Harvey, R. Macarthur, W. Matthews, *Food. Addit. Contam.,* **2002**, 19, 22.
[11] P. Nyman, G. Diachenko, G. Perfetti, *Food. Addit. Contam.,* **2003**, 20, 909.
[12] R. Macarthur, C. Crews, A. Davies, P. Brereton, P. Hough, D. Harvey, *Food. Addit. Contam.,* **2000**, 17, 903.
[13] M. Doležal, M. Chaloupská, V. Divinová, B. Svejkovská, J. Velišek, *Euro. Food. Res. Tech.,* **2005**, 221, 221.
[14] A. Arisseto, E. Vicente, R. Furlani, M. Toledo, *Food. Sci. Tech.(Campinas).,* **2013**, 33, 125.
[15] J. Sun, S. Bai, W. Bai, F. Zou, L. Zhang, Z. Su, *J. Agr. Food. Chem.,* **2013**, 61, 9955.
[16] B. Craft, A. Chiodini, J. Garst, *Food. Addit. Contam.: Part A.,* **2013**, 30, 46.
[17] J. Kuhlmann, *Euro. J. Lipid.. Sci. Tech.,* **2015**, 117, 1.
[18] R. Weibhaar, R. Perz, *Euro. J. Lipid.. Sci. Tech.,* **2010**, 112, 158.
[19] W. Seefelder, N. Varga, A. Studer, G. Williamson, F. Scanlan, R. Stadler, *Food. Addit. Contam.,* **2008**, 25, 391.
[20] K. Hrncirik, Z. Zelinkova, A. Ermacora, *Euro. J. Lipid.. Sci. Tech.,* **2011**, 113, 361.
[21] K. Yamazaki, S. Isagawa, T. Urushiyama, T. Ukena, N. Kibune, *Food. Addit. Contam.: Part A.,* **2013**, 30, 52.
[22] A. Ermacora, K. Hrncirik, *J. Amer. Oil. Chem. Soc.,* **2013**, 90, 1
[23] A. Arisseto, P. Marcolino, E. Vicente, *Food. Addit. Contam.: Part A.,* **2014**, 31, 1385
[24] E. Moravcova, L. Vaclavik, O, Lacina, V. Hrbek, K. Riddellova, J. Hajslova, *Ana. Bio. Anal. Chem.,* **2012**, *402*, 2871.
[25] R. Weibhaar, *Euro. J. Lipid.. Sci. Tech.,* **2008,** 110, 183-186.
[26] A. Ermacora, K. Hrncirik, *J. Am. Oil Chem. Soc.,* **2012**, 89, 211.
[27] C. Crews, P. Brereton, A. Davies, A. *Food. Addit. Contam.,* **2001**, 18, 271.
[28] C. Hamlet, C. *Food. Addit. Contam.,* **1998**, 15, 451.
[29] M. Küsters, U. Bimber, S. Reeser, R. Gallitzendörfer, M. Gerhartz, *J. Agr. Food. Chem.,* **2011**, 59, 6263.
[30] C. Crews, S. Hasnip, S, Chapman, P. Hough, N. Potter, J. Todd, *Food. Addit. Contam.,* **2003**, 20, 916.
[31] V. Christova-Bagdassarian, J. Tishkova, T. Vrabcheva, *Food. Addit. Contam.: Part B.,* **2013**, 6, 163-167.
[32] X. Xu, Y. Ren, P. Wu, J. Han, X. Shen, *Food. Addit. Contam.,* **2006**, 23, 110-119.
[33] X. Xu, H. Wu, H. He, B. Huang, J. Han, Y. Ren, *Food. Addit. Contam.: Part A.,* **2013**, 30, 421
[34] F. Dayrit, M. R. Niñonuevo, *Food. Addit. Contam.,* **2004**, 21, 204-209.
[35] V. DiViNoVá, M. Dolezal, J. Velisek, *Czech J. Food. Sci.,* **2007**, 25, 39.
[36] Z. Zelinková, M. Doležal, J. Velíšek, *Euro. Food. Res. Tech.,* **2009**, 228, 571.
[37] V. Ilko, Z. ZelINkoVá, M. Doležal, A. Velíšek, *Czech J. Food. Sci.,* **2011,** 29, 411.
[38] Z. Zelinková, B. Svejkovská, J. Velíšek, M. Doležal, M. *Food. Addit. Contam.,* **2006**, 23, 1290.
[39] K. Nagy, L. Sandoz, B. Craft, F. Destaillats, *Food. Addit. Contam.: Part A.,* **2011**, 28, 1492.
[40] P. Calta, J. Velíšek, M. Doležal, S. Hasnip, C. Crews, Z. Réblová, *Euro. Food. Res. Tech.,* **2004**, 218, 501.
[41] C.H. Breitling-Utzmann, *Food. Addit. Contam.,* **2005**, 22, 97.
[42] J. Velíšek, M. Doležal, T. Dvoøák, *Czech J. Food. Sci.,* **2002**, 20, 161.
[43] E.F. Authority, *EFSA J.,* **2013,** 1, 3381
[44] K. Hrncirik, G. Duijn, *Euro. J. Lipid. Sci. Tech.,* **2011**, 113, 374.
[45] C. Retho, *Food. Addit. Contam.,* **2005**, 22, 1189-1197.
[46] N. Frank, M. Dubois, G. Scholz, W. Seefelder, J. Y. Chuatv, B. Schilter, *Food. Addit. Contam.: Part A.,* **2013**, 30, 69.
[47] B. Schilter, G. Scholz, W. Seefelder, *Euro. J. Lipid. Sci. Technol.,* **2011**, 113, 309.
[48] V. Divinova, B. Svejkovska, M. Dolezal, J. Velisek, *Czech. J. Food. Sci.,* **2004**, 22, 182
[49] T. Buhrke, R. Weibhaar, A. Lampen, *Arch. Toxi.,* **2011**, 85, 1201-1208.
[50] W.B. Cho, B. Han, K. Nam, K. Park, M. Choi, S. Kim, *Food. Chem. Toxic.,* **2008**, 46, 3172.
[51] S. Mezouaria, L. Yun, G. Paceb, *Food. Addit. Contam.: Part A.,* **2015**, *32*, 768.
[52] T. Haines, K. Adlaf, R. Pierceall, I. Lee, P. Venkitasubramanian, M. Collison, *Am. Oil. Chem. Soc.,* **2011**, 88, 1-14.
[53] A. Ermacora, K. Hrnčiřík, *Food. Addit. Contam.: Part A.,* **2014**, 31, 985.
[54] B. Craft, K. Nagy, L. Sandoz, F. Destaillats, *Food. Addit. Contam.,* **2012**, 29, 354.
[55] M. Ramli, W. Siew, N. Ibrahim, A. Kuntom, R. Razak, *Food. Addit. Contam.: Part A.,* **2015**, 32, 817.
[56] T. Bornscheuer, M. Hesseler, *Euro. J. Lipid. Sci. Tech.,* **2010**, 112, 552.