Review Article

Reaction Path Synthesis of Monoacylglycerol from Fat and Oils

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ABSTRACT

Monoacylglycerol is a typical of lipid compound, which plays a very significant role in food and cosmetic production as well as pharmaceutical industries. It is also categorised as a non-ionic surfactant as it contains a long hydrophobic acyl group and two hydrophilic hydroxyl groups. As a non-ionic surfactant, this compound plays a very essential role as an emulsifier in food industries and as an antimicrobial, antioxidant and anti-atherosclerotic in pharmaceutical industries. It is generally produced through a conventional process known as glycerolysis of oils or fats using inorganic alkaline catalyst at 220-260°C. Numerous approaches have been made to improve this reaction through several process including the enzymatic glycerolysis reaction of oils and fats, transesterification reaction of glycerol with fatty acid esters, alcoholysis reaction of oils and fats, esterification of free fatty acids and glycerol, transesterification reaction of fatty acid ester and esterification of free fatty acids with a protected glycerol compounds such as 1,2-*O*-isopropylidene glycerol and followed by its deprotection reaction using an acid resin such as Amberlyst-15. Monoacylglycerol with highest yield and purity can be produced using 1,2-*O*-isopropylidene glycerol. It is also possible to use specific lipase enzyme (sn-1,3) through ethanolysis reaction of oils, fats and pure triacylglycerols to produce 2-monoacylglycerol.

Keywords: monoacylglycerol, fat, vegetable oil, fish oil.

INTRODUCTION

Monoacylglycerol or monoglyceride is a typical of compound which belongs to the class of lipids containing one ester group (-COOR) of long chain fatty acid and two hydroxyl groups (-OH) attached to propane chain. If the ester group is attached to C_1 and the two-hydroxyl groups are attached to C2 and C3 of the propane, the compound is called 1-monoacylglycerol. Conversely, if the ester group is attached to C2 while the two-hydroxyl groups attached to C1 and C3, the compound is called 2-monoacylglycerol. Figure 1 shows the chemical structure of a typical of monoacylglycerol:

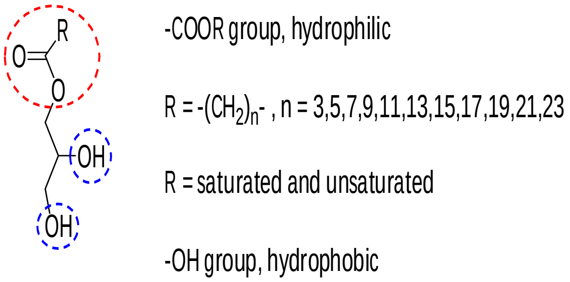

Figure 1: Chemical structure of a monoacylglycerol

It is generally known that hydrophilic properties of a monoacylglycerol is due to the presence of two hydroxyl group while its hydrophobicity is determined by a non polar acyl groups from its ester parts. The combination of both properties in a monoacylglycerol has determined its wide range of applications among which as an emulsifier. Almost of types of monoacylglycerol can be applied in pharmaceutical, cosmetics and food industry[1]. This compound can also be used as a non-ionic surfactant and as a precursor in the synthesis of active lipids such as triglycerides, diglycerides, phospholipids, glycolipids, and lipoproteins[2]. There are also several additional applications of monoacylglycerols including lubricating agents, plasticisers, and additives in textile manufacturing process[3]. Some specific monoacylglycerols have also been identified to have specific activities such as monolaurin as an antibacterial, anti fungi and antiviral agents[4-8] and monoolein as an antioxidant[9].

Monoacylglycerols from polyunsaturated fatty acids such as eucosapentanoic acid (EPA) and docosahexanoic acid (DHA) have been identified to have a high nutritional value, which contribute to the human being's health[2,10].

Commercial monoacylglycerol are usually produced conventionally through what so called continuous glycerolysis reaction of oils or fats. The rate of this reaction is generally accelerated by the addition of inorganic base catalysts such as NaOH, KOH, $Ca(OH)_2$, and takes place at a very high temperatures of 220-260°C under continuous flow through of nitrogen gas[11].

The yield of monoacylglycerol produced through this reaction ranges from 10 to 60% and depends on the conditions of the reaction such as the molar ratio between oil and glycerol. Some previous research also reported that chemically glycerolysis oils and fats can result in the production of monoacylglycerol, diacylglycerol and triacylglycerol with the composition of 45-55%, 38-45% and 8-12% respectively[12]. Further molecular distillation would then be required to obtain monoacylglycerol with the purity of 90%[1], which is needed in food and pharmaceutical industries.

Apart from its high purity requirement in both food and pharmaceutical industries, there are also several disadvantages from synthesising monoacylglycerol through glycerolysis including high-energy consumption, its charred flavour and its dark colour. In addition, this synthesis path is not suitable for producing a heat resistant monoacylglycerol such as those containing polyunsaturated fatty acids like EPA and DHA[11].

Monoacylglycerol is also a multi functional lipid compound that can easily be synthesised from abundant natural resources such as vegetable oils and animal fats. As a non-ionic surfactant, this compound plays a very essential role as an emulsifier in food industries and as an antimicrobial, antioxidant and anti-atherosclerotic in pharmaceutical industries. Despite its high industrial demand, its availability on the other hand is very limited which is due to several weakness in its synthesis path mainly through glycerolysis reaction of vegetable oils and fats.

In this review article, it will be discussed several synthesis path of monoacylglycerol from vegetable oils and fats. It will also be reviewed several new approaches developed for the improvement of synthesising monoacylglycerol from oils and fats. There are some existing methods to synthesis monoacylglycerol from vegetable oils and fats including glycerolysis, alcoholysis, esterification of glycerol with a free fatty acid, esterification of free fatty acids and transesterification of fatty esters with a protected glycerol compound namely 1,2-*O*-isopropylidene glycerol. Majority of these reactions can be accelerated with catalysts such as inorganic base compounds and lipase enzyme.

Glycerolysis of Oils and Fats

Glycerolysis is a chemical reaction of breaking down triglyceride molecules of oils or fats with the use of glycerol to produce monoacylglycerol or diacylglycerol. This reaction is generally is accelerated by base catalysts. This reaction is also known as interesterification reaction and can be described as shown in figure 2.

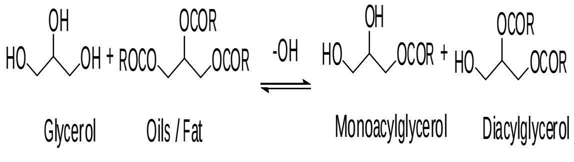

Figure 2: Glycerolysis reaction of oils and fats with the use of base catalysts

In industry, this process is usually conducted at 200°C with the use of NaOH and KOH as the catalysts. The application of high temperature in this reaction generally results in the generation of some chemical impurities, which leads to the production of low quality of monoacylglycerol. The characteristics of the monoacylglycerol generated through this reaction are including burned smells and dark colour, which indicate its disadvantages to be used in food industries[10]. These short comings have been reported to be overcome by the use of $Ca(OH)_2$ as the catalysts in which the monoacylglycerol produces is colourless[13].

It has been reported that in addition to diacylglycerol and triacylglycerol, monoacylglycerol can also be produced from sunflower oil with the use of $Ca(OH)_2$ as the catalysts. Further result of HPLC analysis showed that this reaction could generate monoacylglycerol with the purity of 48.3% with monoolein and monolinolein as the highest compositions[14]. Numerous papers have also reported the successful synthesis of monoacylglycerol from rapeseed oil through glycerolysis reaction with the use of heterogenous base catalysts such as Cs-MCM-41, Cs-sepiolite, MgO, and calcined hydrotalcite with different Al/Al + Mg ratios. These heterogenous catalysts have a fairly high degree of alkalinity with pKa values ranging from 9 to 16. As has been reported, the use of MgO catalysts could result in the generation of α-monoacylglycerol from rapeseed oil with the highest yield at 65%[13]. In addition, glycerolysis of methyl stearate and tristearin have also been carried out to produce monostearin with the use of non ionic alkaline catalysts which are strong bases of alkyl guanidine compounds such as 1,5,7-triazabicyclo[4.4.0]dec-5-ene, 1,2,3-tricyclohexylguanidine, and 1,3-Dicyclohexyl-2-n-octylguanidine. Interestingly the application of these types of catalysts with the amount of 10% could result in the production of monostearin with the purity of higher than 90% in 6 hours of reaction time[15].

Enzymatic Glycerolysis of Oils and Fats

Recent research has shown the successful application of enzymatic catalysts as a potential substitute for conventional inorganic base catalysts in glycerolysis reaction. This reaction has been reported to take place at low temperatures (< 80°C) in order to produce monoacylglycerol, which has a very good quality and is sensitive to heat. However, this process has also a variety of drawbacks including long reaction time, low reactant conversion factor, high cost and unavailability of the enzymes. Also, in some cases, it has been found that enzymatic glycerolysis reaction has low efficiency which is mostly caused by the inhomogenities between oils or fats with lypophilic properties respectively and lipase enzyme with hydrophilic properties if the reaction conducted at low temperatures. Therefore, it is very important to consider a suitable solvent in order to maintain homogeneity between oils or fats and the enzyme. Figure 3 shows enzymatic glycerolysis reaction of oils and fats.

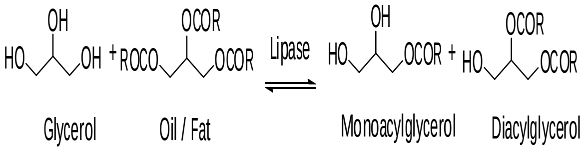

Figure 3: Enzymatic glycerolysis reaction of oils and fats

McNeill for example, have successfully conducted a glycerolysis reaction between some samples of oils and fats and glycerol using lipase enzyme as the catalyst without any use of solvents and emulsifiers in a batch system[16]. It has also been reported that the products of this reaction from all different oil and fat samples are mixtures of monoacylglycerol, diacylglycerol and triacylglycerol. Monoacylglycerol with the highest yield of 90% could be generated from glycerolysis reaction of olive oil, while the lowest yield of 30% could be produced from hydrogenated lard. Similarly, glycerolysis reaction of butter fat has been carried out by Garcia. Using lipase enzyme obtained from *Pseudomonas cepacia* in a solvent-free systems[17]. The reaction was reported to take place at a temperature of 40°C with a ratio of butter fat to glycerol of 2 to 1. With the addition of 1% lecithin and a water content of 10.5%, it could be produced mono and diacylglycerol with the average yield of 70%.

Different catalytic approach of glycerolysis reaction of the olive oil has been successfully carried out by Rosu. Using lipase enzyme immobilized on varieties of materials such as$CaCO_3$, $CaSO_4{\cdot}2H_2O$, $Ca_2P_2O_7$ and celite as solid suports[18]. It was reported that the use of lipase enzyme from *Pseudomonas sp*. which was immobilized on $CaCO_3$ as support was able of producing monoacylglycerol with a purity of 90%. This reaction was found to occur for 72 hours and the enzyme was chemically active for use up to 5 cycles of reactions. Several other research have also revealed the successful use $CaCO_3$ material as a support for the immobilization of lipase enzyme obtained from other bacteria such as *Chromobacterium viscosum* lipase and Pseudomonas pseudo alkali. The study of glycerolisis of soyoil using lipase enzymes obtained from nine different sources has also been successfully carried out in the year 1998 by Noureddini dan Harmeier[19]. Lipase from *Pseudomonas sp*., for example, was able to catalysed a production of monoacylglycerol with the highest yield. This result, specifically, can be achieved by adjusting the conditions of a reaction such as temperature of 40°C, glycerol to oil ratio of 2 to 1, the enzyme to oil ratio of 0.1 to 10, and are reaction time of 1 hour.

Recent publication has shown that glycerolysis of palm oil and palm kernel oil at a temperature of 40°C has been successfully carried out by incorporating lypaze enzyme obtained from *Humicola lanuginosa* as a catalyst. This reaction was conducted by adjusting the ratio of oil to glycerol as 0.5 without any additional solvent[20]. The result of TLC-FID of the reaction's products indicated the presence of monoacylglycerol after 24 hours. It was found that glycerolysis of both palm oil and palm kernel oil can result in the production of mono acyl glycerol with a yield of 18% and 31%, respectively. Kaewthong in 2005 have also tested 9 types of lipase enzymes to catalyse the production of monoacylglycerol from glycerolysis of palm oil. In that research, they found out that the one from *Pseudomonas sp*. was the best to catalyse glycerolysis reaction at 40°C and yielded 28.5% of monoacylglycerol[21]. They also found that Accurel EP-100 (<200 m) was a suitable support material for the immobilization of *Pseudomonas sp*. which could best give hydrolytic activity of 10 : 42 U/mg. Further glycerolysis experiment of tuna oil with the use of lipase AK enzyme derived from *Pseudomonas fluorescence* which was immobilized on Accurel EP-100 (IM-AK) could produce monoacylglycerol. This monoacylglycerol produced through this reaction was rich in poly unsaturated fatty acids (PUFA), namely eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA)[22]. It was reported that methyl *tert*-butyl ether (MTBE) was the best solvent for this reaction and in the optimum condition monoacylglycerol can be produced with the highest yield of 24% containing PUFAs such as EPA amd DHA by 56%. Monoacylglycerol can also be generated through glycerolysis of olive oil with the use of novozym 435 as the catalyst, sodium (bis-2-ethyl-hexyl) sulfosuccinate (Aerosol-OT/AOT) as a surfactant and a propane pressurized as the solvent[23]. This reaction was a very potential reaction route for the production of monoacylglycerol. Diacylglycerol can also be produced at a moderator reaction conditions (mild condition) such as temperature of 30°C, pressure of 30 bar, ratio of solvent to substrate as 4 to 1 and total reaction time of 1 hour.

The effectiveness of using several solvents both as a single and mixture with different typical of polarity has been assessed by Dasmtrup in glycerolysis reaction of sunflower oil sample using lypaze enzyme of novozym 435[12]. As a single solvent, *tert*-butanol and *tert*-pentanol are found to be very suitable for a quick glycerolysis of sunflower oil with a yield of 68-82% of monoacylglycerol. It was also reported that the use of two solvent mixture such as *tert*-butanol/hexane, *tert*-pentanol/hexane, and *tert*-butanol/*tert*-pentanol in similar reaction can lead to the production of monoacylglycerol with a yield of 58-75%. Similar result was also reported by Zhong where they successfully utilised the mixture of *tert*-butanol and isopropanol as solvents in glycerolysis reaction[10]. In this research, they showed that the optimum amount of monoacylglycerol of 72% could be achieved when using *tert*-butanol and isopropanol with the ratio of 80 to 20, 15% (w/w) of Lipozim TL IM, 10% (w/w) of glycerol water content, solvent to oil ratio of 4 to 1, and molar ratio of glycerol to oil of 3 to 5, with the reaction time of 4 hours. Utilising Babasu oil, Freitas have shown a successful synthesis of monoacylglycerol through glycerolysis[24]. This reaction was based on the use of lipase enzyme obtained from *Burkholderia cepacia* which was immobilized on poly vinyl alcohol composite. The maximum amount of monoacylglycerol which can be generated through this reaction was found to be 25% where there were several special reaction condition such as mole ration of oil to glycerol of 1 to 15 and a temperature of 55°C.

The production of monoacylglycerol as an emulsifier has also been successfully carried out by Naik in which they utilised *tert*-butanol as a solvent and Fermase CALB 10000 enzymes as the catalyst[11]. The optimum conditions for the production of monoacylglycerol as reported by Naik were the mole ratio of oil to glycerol as 1 to 5, the amount of enzyme by 15% (w/w) of the total amount of reactants, and 5 hour reaction time. Under the optimum conditions, it is reported that monoacylglycerol could be produced in the yield range of 70-80%. Castrol oil which is generally known to be rich of ricinoleic acid has also been used to produce monoacylglycerol which contains monorisinolein[25]. Glycerol and NaOH based catalyst used in this reaction were derived from the mixture of aqueous phase which was a residual phase from the purification of biodiesel. The result of Gas Chromatography analysis indicated that this by product of biodiesel purification from contains 88.1% of glycerol and 1.7% (w/w) of NaOH. It was found that the maximum amount of monoacylglycerol of 50.4% could be generated through this reaction at a temperature of 180°C and reaction time of 30 minutes. Zhang (2014), using partially hydrogenated corn oil, has successfully carried out a glycerolysis reaction with the use of a combination Al_2O_3 and K_2CO_3 as the catalyst[26]. Molecular distillation technique was further applied in order to obtain monoacylglycerol with higher purity than 90%. Further report has shown that vegetable oil such as Karanja seeds oil could also be used as an oil source for the production of monoacylglycerol. Karanja seeds oil, as has been reported to contain 53.52% of oleic acid, can react with glycerol at a temperature of 230°C to produce monoolein as the largest component of monoacylglycerol. This reaction was reported to happen faster in the presence of PbO (litharge) as a catalyst[27].

Reaction of Glycerol and Fatty Acid Esters

Monoacylglycerol can also be generated through the reaction of glycerol with a fatty acid ester with the use of either acid or based catalysts. Currently, many research are focusing on the use of heterogeneous acid-base and enzymatic catalysts in this process, as a means of implementing *Green Chemistry*. Figure 4 shows a glycerolysis reaction scheme of a fatty acid ester.

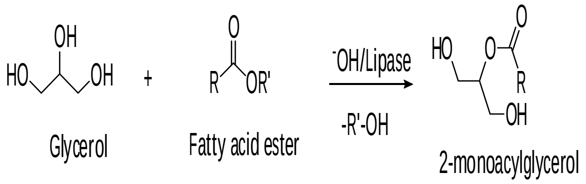

Figure 4: Glycerolysis reaction of fatty acid ester

Heterogeneous MgO base catalyst has been applied in the synthesis of monoolein from the reaction of glycerol with methyl oleate[28]. The maximum yield of monoaclyglycerol produced through this reaction was found to be in the range of 73 to 77% which can be achieved when the reaction takes place at high temperatures of 220-250°C, the molar ratio of glycerol to methyl oleate between 2 to 6, ratio of catalyst to reactant as 30 g/mol and a reaction time of 2 hours. It has also been successfully carried out a glycerolysis reaction of glycerol with methyl oleic with the use of similar catalysts containing different amount of Li[29]. It was found that the presence of Li in the catalysts can raise the level of MgO basicity, which can lead to the production of monoacylglycerol with a yield of 70-72% at a temperature of 220°C. Ferreti for example, has studied a glycerolysis reaction of glycerol with methyl oleate in the presence of MgO as the catalysts in the liquid phase to produce mono acyl glycerol experimentally and with the use of density functional theory[30]. The result of catalytic activity showed that a strong foundation in terms of kinetics for this reaction step was due to the low surface coordination of O^{-2}. Further analysis indicated that the main product from this reaction was 1-monoolein. Similar reaction product of monoacylglycerol has also been successfully produced through the reaction between glycerol and methyl esters which were from the product of transesterification reaction of castrol oil[25]. The optimum condition for the production of the maximum yield of monoacylglycerol (45%) was found either at a reaction temperature of 180°C for 20 minutes or a temperature of 200°C for 5 minutes.

Alcoholysis of Oils and Fats

It has been reported that alcoholysis of oils and fats is one of the synthesis pathways to produce monoacylglycerol. This synthesis path incorporates the reaction between triglycerides of oils and fats and primary alcohols such as methanol and ethanol. This reaction is often known as a partial transesterification reaction of triglycerides with the use of limited amount of alcohol and is catalyzed by a weak base or lipase enzymes. Figure 5 shows the typical alcoholysis reaction of oils and fats.

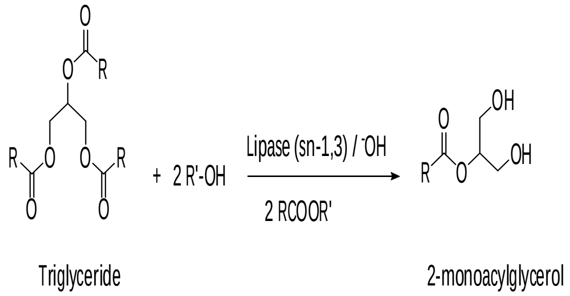

Figure 5: Alcoholysis reaction of triglyceride from oils and fats

Synthesis of 2-monoacylglycerol has been carried out by the reaction of 0.56 mmol of triglyceride from peanut oil with 5.6 mmol dry ethanol using an anzymatic catalyst of lipase enzyme from *Rhizopus delemar* species as the catalyst and methyl *tert*-butyl ether as the solvent[31]. The obtained crude product was further purified by crystallization using n-hexane/MTBE (70:3 v/v) at a temperature of -25°C for overnight to produce 71.8% yield of monoacylglycerol. Alcoholysis reaction of some triglycerides such as triacetin, tributyrin, tricaproin, tricaprylin, trilaurin and tripalmitin has also been reported to be catalyzed by an anzymatic lipase obtaine from *Pseudomonas fluorescens* species in ethanol and dried butanol[32]. This research revealed several types of solvents which were suitable to produce monoacylglycerol with different maximum composition such as n-butanol for the production of 85% monoacetin, ethanol and n-butanol for the production of 96% monobutyrin, n-butanol for the production of 50%

monocaprylin, isopropanol for the production 48% of monolaurin and 45% of monopalmitin.

Synthesis of 2-monoacylglycerol rich in poly unsaturated fatty acids has also been carried out through the alcoholysis reaction of fish oil with ethanol and catalysed by lipase enzyme of Novozym 435[33]. As has been reported, the use of excessive amount of 96% ethanol can result in the production of 2-monoacylglycerol with the yield of 90.3%. Esteban for instance, has done the synthesis of 2-monoacylglycerol through the ethanolysis reaction of cod and tuna oils using lipase enzyme as the catalysts in two different reactors which were stirred tank reactor (STR) and packed bed reactor (PBR)[34]. The highest yield of 2-monoacylglycerol (68.2%) was achieved in the use of STR in the optimum reaction conditions such as 500 mg of tuna fish oil, 500 mg of dry ethanol, 3 mL of acetone, 1: 1,5 of lipase DF and MP-1000 (w/w), stirring speed of 200 rpm and a temperature of 37°C for 24 hours. 2-monoacylglycerol of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) could be each produced with a yield of 40 and 45% from both tuna and cod oil.

The synthesis of 2-monoacylglycerol through alcoholysis of cod liver oil has been done by Rodriques using Novozym 435 lipase from Candida antartica and DF of *Rhizopus oryzae*[35]. Using 96% ethanol as the solvent and lipase enzyme of Novozym 435 type, it was found that 2-monoacylglycerol could be produced with a yield ranging from 54 to 57%. After purification through an extraction using ethanol and n-hexane, 2-monoacylglycerol purity was almost double to its highest points of 96.4% and 83.9%. Alcoholysis of palm oil have also been conducted using a limited methanol with its ratio to palm oil was 1 : 2.1[36]. This alcoholysis reaction took place at 65°C and was catalysed by a weak base catalyst K_2CO_3 as much as 0.25% (w/w) of the total amount of the reactants. This reaction generated a mixture of monoacylglycerol with a yield of 38%. Soto (2014) in their recent paper, reported a partial transesterification of sunflower oil using supercritical methanol[37]. The reaction was conducted at a range of temperature of 283-292°C with methanol to oil ratio of 20 : 50. The result of products' reactant analysis indicated that there was a mixture of monoacylglycerol and diacylglycerol with a yield of 99.8% obtained from this reaction.

2-monoolein compounds in the form of its isomers with the composition of 9 to 1 and a yield of 76% have been successfully synthesized through ethanolysis reaction of triolein using lipase enzyme from *Rhizopus oryzae* types[38]. This reaction was able to take place in an aqueous solvent or organic solvents two phases which lead to a high reaction rate based on the interfacial activation of lipases. The synthesis of 2-monoacylglycerol through ethanolysis reaction has also been done by Rahman in which they reacted 1 mol of canarium oil and 4 mol of ethanol using lypaze enzyme obtained from *Mucor miehei* as the catalysts[39]. Further purification of the reaction product by solvent extraction using hydroalcoholic solvents resulted in the production of 74% of monoacylglycerol which is rich in monoolein and monolinolein. Wang in their paper published in 2014 reported the use of ethanolysis reaction to produce monoacylglycerol from arachidonic acid-rich oil using novozym 435 as the catalyst[40]. In this paper, they also summarized the optimum conditions for the enzymatic transesterification such as type of solvents, the amount of lipase, and the duration of the reaction. The optimum conditions for the reaction has been found to be 35% (w/w) of lipase enzyme, 2 hour reaction time, and the use of ethanol as the solvent. The yield of crude 2-monoacylglycerol produced when applied the optimum conditions was around 31.4%. Further purification process by solvent extraction and crystallization in n-hexane, 79.4% of 2-arachidonoyl glycerol was obtained at 42.9% 2-monoacylglycerol yield.

Esterification of Glycerol with Free Fatty Acids

Chemical Esterification

Monoacylglycerol can also be synthesized through a direct esterification of free fatty acids and glycerol using acid catalysts either homogenous or heterogeneous. Figure 6 shows the typical esterification reaction with acidic catalysts.

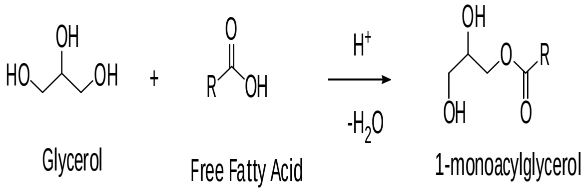

Figure 6: Esterification of free fatty acids with glycerol using acidic catalysts

It has been reported the successful esterification of 1 to 1 ratio between lauric acid and glycerol using 0.5% (w/w) of sillated sulfonate mesoporous (MCM-41-SO_3H) as the catalysts at a temperature of 112°C. This reaction resulted in the production of monoacylglycerol with a yield of 53%[41]. It was also reported that using an Amberlyst-15 as the catalysts and under similar optimum conditions, monoacylglycerol in the form of monolaurin only can be produced with the yield of 44%. The successful application of MCM-41 hybrid materials as the catalysts in this reaction was due to the fact that it contains alkyl (methyl and propyl) and sulfonic acid simultaneously which can act as a catalyst in the esterification of glycerol with either lauric acid or oleic acid[42]. By maintaining the ratio between methyl groups to the sulphonic acid and applying the optimum conditions of the catalyst, monolaurin and monoolein compounds can be generated with a yield of 63% and 45% respectively. Further work published by Diaz in 2002 has also revealed the synthesis of MCM-41 material containing mercaptopropyl (methyl) silanes as a catalyst for the esterification of glycerol with either lauric or oleic acid[43]. Further research by Diaz published in 2002 have also been synthesized MCM-41 material containing mercaptopropyl (methyl) silanes as catalyst esterification reaction of glycerol with lauric acid and oleic acid[43]. They also reported that the selectivity formation of monolaurin and monoolein by catalysts containing the new silane functional groups is higher than either methyl group or sulfonic acid attached to the free Si atom.

Recent research has reported the application of aluminium and zirconium containing MMS-H mesoporous material as the catalysts in the esterification of lauric acid and glycerol in supercritical CO_2 conditions[44]. This catalyst was able to convert lauric acid into both monolaurin and dilaurin in the equal amount with the conversion rate of 93%. Synthesis monolaurin through esterification of lauric acid with glycerol have also been conducted by Nakamura using metal salts of multi valence as the catalysts[45]. It was reported that $ZrOCl_2\cdot 8H2O$ and $AlCl_3\cdot 6H_2O$ based catalyst were able to produce monolaurin with a high degree of selectivity. The use of H_2SO_4 as a homogeneous catalyst in the synthesis of monolaurin has also been reported by Widiyarti in their recent paper published in 2009[46]. As has been reported, the optimum conditions for this reaction were 1 to1 ratio of glycerol and lauric acid, 5% (w/w) from the total reactants of H_2SO_4 as the catalysts, 6 hour length of reaction time and 130°C of the reaction temperature. Monolaurin and dilaurin produced each had a yield of 31.05% and 4.48% after going through the process of purification by column chromatography techniques. It was found that after the purification by using column chromatography, the ratio between monolaurin and dilaurin was 30.05% and 4.48%.

A new finding has revealed the successful application of complexes catalysts of solid Fe-Zn double metal cyanide (DMC) which has very high activity in the esterification of free fatty acids with glycerol[47]. The types of monoacylglycerol generated through this reaction were 66% of monolaurin, 75.9% of monomiristin, 62.2% of monostearin and 63.4% of monoolein. This result was achieved on the conditions of 1 to 1 ration between lauric acid and glycerol, 0.21 gram of the catalyst, at a temperature of 180°C for 1 hour reaction. The kinetics model of esterification of lauric acid with glycerol has also been studied using a catalyst propyl sulfonic acid functionalised mesoporous materials SBA-15 in a reduced pressure conditions[48]. The amount of monoacylglycerol was found to increase with the increasing of temperature, amount of catalyst and the molar ratio of between the reactants.

Direct esterification of residual vegetable oil waste which contains free fatty acid (lauric acid) with glycerol is another alternative to produce monoacylglycerol. The Optimum conditions have been reported to be 1 to 1 until 1 to 3.1 ratio between lauric acid and glycerol, 2 to 8% of two layers of hydroxide catalyst Mg-Al-CO_3, variations in the temperature from 100-180°C for 2 hours[49]. The conversion rate to produce monolaurin and dilaurin from glycerol was reported to be 99%. Heterogeneous catalysts SBA-15 functionalised by 12-tungstofosfat acid have been successfully synthesized by Hoo and Abdullah and applied in esterification of lauric acid with glycerol[50]. It was found that 70% of acid can be converted to generate monolaurin with a yield of 50% in 6 hours of reaction time using 20% (w/w) of the catalysts at 160°C. This reaction has been optimized by using Taguchi Orthogonal approach where it was conducted in a special reactor and radiated by either far (2700-30000 nm) and near (360-2000 nm) infrared irradiation [51]. At its optimum conditions of 80°C, 6 to 2 molar ratio between glycerol to lauric acid, 900 rpm of the stirring speed, 5% (w/w) of the catalyst and under infrared radiation, the conversion rate of lauric acid can reached 99%. Under similar optimum conditions but with, the conversion rate of lauric was found to slightly decrease to 97.6%.

Enzymatic esterification

Different approach to synthesize monoacylglycerol from free fatty acids and glycerol has been made by incorporating a new type of catalyst, which is a lipase enzyme. Figure 7 shows the esterification reaction between glycerol and free fatty acids catalysed by lipase enzyme.

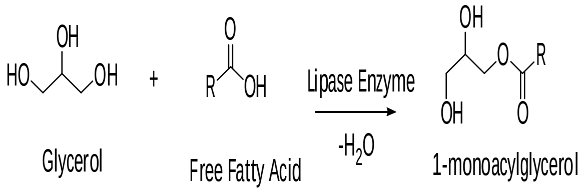

Figure 7: Esterification reaction of free fatty acids and glycerol using lipase enzyme

Proteins extracted from potatoes have been known to contain lipid acyl hydrolase (LAH) enzyme which has been successfully applied in the synthesis of monoacylglycerol from capric acid, lauric acid, myristic acid, linoleic acid and linolenic acid[52]. By eliminating the water using a reduced-pressure distillation techniques, the yield of monoacylglycerol production from glycerol and each of the fatty acids can be increased with a conversion rate of each fatty acid more than 95%. Yeh and Gulari, for example, studied the esterification of lauric acid with glycerol (water content of 50% (w/w)) using *Rhizomucor miehei* lipase as the catalyst in a foam reactor[53]. They reported that both monolaurin and dilaurin can be generated through this process with an average yield of 80%.

A new research has reported the synthesis of monocaprin, monolaurin and monomiristin without any additional solvents catalysed by using Lipozym IM-20 enzymes[54]. The highest yield of monoacylglycerol was achieved when the molar ratio of glycerol to fatty acids was 1 to 1, the amount of the enzyme was 9% (w/w) and the temperature reaction was at 60°C. After 5 hours of reaction, it was found that the reaction product contained monoacylglycerol two times higher than diacylglycerol with all the conversion rate reaching 80% of the fatty acids. It has also been reported the optimization study of monolaurin synthesis from lauric acid and glycerol using a Lipozym IM-20 enzyme catalyst without any additional solvent[55]. The highest yield was best achieved at a reaction temperature of 55°C, the ratio of glycerol to lauric acid of 1 to 1, and the amount of lauric acid catalyst of 3% (w/w). After 6 hours of reaction, the products was found contain the mixture of acylglycerol including 45.5 % of monolaurin, 26.8% of dilaurin (26.8%), 3.1% of trilaurin and 24.6% of lauric acid. Monoacylglycerol has also been synthesised from the reaction of glycerol and fatty acids obtained through a distillation of enzymatic hydrolysis of palm oil and palm kernel oils with levels of 75.2% and 76.2% respectively[56]. This reaction is catalysed by lipase Lipozym RM IM enzyme, and the yield of monoacylglycerol produced from fatty acid fraction of both palm oil and palm kernel oil were in the range of 18.8 to 22.9% and from 19.1 to 22.5% respectively.

A new research finding has recently reported the synthesis of monolein using lipase enzyme from *Staphylococcus simulans* species which was immobilized on $CaCO_3$ as the solid support[57]. This report has also revealed that this approach has resulted in a very good catalytic activity during the production of monoacylglycerol. As indicated by the report, the amount of monoolein produced through this reaction was 70% in its optimum conditions such as 100 IU of the enzyme, molar ratio of oleic acid to glycerol of 0.2 and the amount of water added as 5% (w/w). In their very recent paper, Freitas (2010) described the synthesis of 1-monoacylglycerol through the esterification reaction of lauric acid, myristic acid, palmitic acid, stearic acid and oleic acid with glycerol using a lipase enzyme obtained from *Penicillium camembertii* which was immobilized on epoxy SiO2-Poly Vinyl Alcohol composite[58]. After 6 hour reaction, the composition of monoacylglycerol produced was of 59.45% monolaurin, 47.92% monomiristin, 45.86% monopalmitin, 42.16% monostearin and 32.92% monoolein. Another interesting finding has reported the successful synthesis of 1-monocaprin through a reaction of a capric acid with glycerol using *Calotropis procera* R. Br. *Carboxylesterase*[59]. As has been reported, bis (2-ethylhexyl) sodium sulfosuccinate and isooctane were suitable and effective surfactant and organic solvent for the formation of 1-monocaprin in reversed micelles.

The production of monoacylglycerol through esterification of lauric acid with glycerol has been successfully done with the help of lipase *Candida sp. 99-125* enzyme with the addition of beta-cyclodextrin[60]. In its optimum reaction time of 8 hours, the yield of monoolein obtained was 46.6% with a purity of 90%. Another recent report has revealed the successful esterification of palmitate acid with glycerol in the CO_2 expanded acetone system at a temperature and pressure of 40-60°C and 65-85 bar, respectively[61]. The maximum yield of monoolein from this research was obtained when the temperature, pressure and amount of enzyme relative to oleic acid were 25°C, 85 bar and 25% (w/w), respectively. Further research on the synthesis of monoacylglycerol has shown that type B lipase enzyme of *Candida antartica* which was cross-linked with glutaraldehyde was able to catalysed palmitic acid reaction with glycerol to produce monopalmitin with a yield of 87%[62].

Synthesis of monocaprin and monocaprylin without any additional solvent has been done by Wan using novozym 435 in an enzyme packed bed reactor system (EPBR)[63]. Without either molecular sieves or a vacuum system, the highest caprylic acid conversion reached was 90.2% in 4 hour reaction time. Under the same conditions, 88% of caprylic acid can be converted using enzyme batch reactor (EBR) in 9 hour reaction time. In a new research, Huang have discovered a new enzyme for the synthesis of monoacylglycerol from *Penicillium cyclopium* which was expressed in Pichia pastoris strains GS115 and generally known as Lipase GH1[64]. Using this enzyme, it was found that the conversion rate of oleic acid can reach 84% when it was reacted with glycerol in 1 to 11 ratio for 24 hours. It was also important to note that under this optimum condition, the water content of glycerol should be maintained to be 1.5% (w/w), the amount of the enzyme to be 80 U/g, and the temperature reaction of 35°C. Based on the result, it can be inferred that lipase GH1 enzyme has a higher activity than the G50 in the esterification of free fatty acids with glycerol to produce monoacylglycerol.

Reaction with Protected Glycerol

One of the disadvantages to synthesize monoacylglycerol through the esterification reaction between glycerol and free fatty acids was the co occurance of continuous acylation reaction for another OH group of the glycerol to form a diacylglycerol and triacylglycerol. In order to overcome this problem, some studies employ the use of a protected glycerol in the production of monoacylglycerol. This is considered to be a very promising method to obtain 1-monoacylglycerol compound with high yield and purity. One among all protected glycerol compounds that is very well-known is produce 1,2-O-isopropylidene glycerol or 1,2-acetonide glycerol. This compound can be synthesized from the reaction of 1 mmol glycerol in 20 mmol acetone with a pTSA as the catalyst[65]. In the end of the reaction, H_2O molecules formed as the reaction by-product can be removed using Dean Stark Water Collector equipment. Further neutralization of the pTSA catalyst using weak base such as Na_2CO_3 was able to produce 1,2-O-isopropylidene glycerol with a yield of 94%.

It has been reported that the transesterification of an ester fatty acids with a protected glycerol compounds such as produce 1,2-O-isopropylidene glycerol using either an inorganic base or enzyme lipase as the catalyst can result in the production of ester compound of a protected glycerol. Subsequently, this protected glycerol can be deprotected using an acid catalyst to generate 1-monoacylglycerol. Figure 8 shows a transesterification reaction of a fatty acid ester with produce 1,2-O-isopropylidene glycerol followed by its deprotection stage with acid resin.

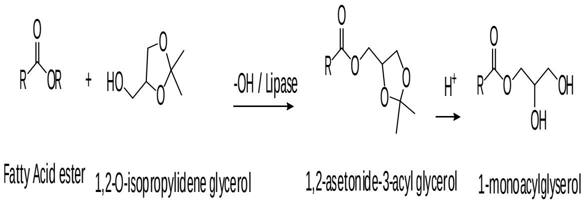

Figure 8: Transesterification reaction of 1,2-O-isopropylidene glycerol with fatty acid ester

Transesterification reaction of 1 mmol methyl stearate with 1.3 mmol of 1,2-O-isopropylidene glycerol using a 0.1 mmol of Na_2CO_3 as the catalyst for 6 hours was reported as an effective path for producing 1,2-*O*-isopropylidene glycerol stearate with a purity of 97%[65]. During the transesterification reaction, methanol as a by product can be removed from the container through an atmospheric pressure evaporation. The deprotection of isopropyliden glycerol stearate compound with an Amberlyst-15 in ethanol for 6 hours can result in the production of glycerol monostearate with a purity of 97%. In their recent paper, Junior described the synthesis of monostearin through the esterification reaction of stearic acid with 1,2-O-isopropyliden glycerol using lipase enzyme types Lipozim RM IM as the catalyst. This reaction was done using surface response method[66]. It was also reported that the deprotection of the reaction product was done using boric acids. The conversion rate of stearic acid into monostearin reached 95% after the reaction for 4 hours.

A very recent publication has successfully revealed the esterification reaction of palmitic acid with 1,2-acetonide glycerol using novozym 435 as a catalyst. This reaction was further followed by its product's deprotection using Amberlyst-15[67].

Repeated recrystallization was carried out to obtain pure 1-monopalmitin. Similar reaction to generate monopalmitin through a trasesterification of glycerol was also carried out with the use of novozym 435 as the catalysts. In this study, it was found that Novozym 435 was a highly active enzyme which was suitable for the transesterification reaction of vinyl palmitate with glycerol without any absorption of glycerol on silica gel. Another study has reported the synthesis of monostearin from the reaction of stearic acid with 1,2-O-isopropyliden glycerol using lipase enzyme obtained from *Candida antarctica* B which was immobilized on a bis (2-ethylhexyl) sodium sulfosuccinate system and isooktan as surfactants and organic solvents respectively[68].

This reaction was carried out at a temperature of 40°C and after 30 minutes monostearin was produced with a yield of 80%. Synthesis of monoolein from the reaction of oleic acid with 1,2-acetonide glycerol has also been successfully conducted by Wang using novozym 435 as the catalysts followed by its deprotection using Amberlyst-15[2]. After recrystallization using n-hexane, it was found that 1-monoolein can be obtained with a yield of 72.8% and a purity of 96.2%.

CONCLUSION

Monoacylglycerol is a nonionic surfactant compounds which can be derived from vegetable oils or fats. Two hydroxyl groups and a long chain acyl group in monoacylglycerol allow these compounds to have a very important applications in the food, pharmaceuticals and cosmetics industries. In the pharmaceutical field, monoacylglycerol compound has potential as an antimicrobial activities such as antibacterial, antiviral, antifungal, antiprotozoa. Moreover, this compound has also been reported to have an antioxidant activity. Monoacylglycerol obtained from poly unsaturated fatty acids such as EPA and DHA has been known to have the function as an essential nutrient for human health.

It has been revealed throughout this paper that there were several disadvantages associated to the production of monoacylglycerol through glycerolysis of vegetable oils or fats such as high energy consumption, low product quality and requirement of a complicated product purification techniques. Various approaches have been made to this reaction route in order to overcome these disadvantages of this process such as an enzymatic glycerolysis of oils and fats, the transesterification reaction of glycerol with fatty acid ester, alcoholysis of oils and fats, esterification of free fatty acids and glycerol by chemical catalysts and lipase enzymes. Also the development has been made through the transesterification reaction of fatty acid esters and esterification of free fatty acids each with by a protected glycerol compound such as 1,2-O-isopropyliden glycerol or 1,2-acetonide glycerol which was followed by deprotection stages. It was clearly revealed that Amberlyst-15 compound was found to be an effective acid resin to deprotect acetonide groups in order to produce two hydroxyl groups on glycerol. Further explanation has shown that monoacylglycerol with highest purity and yield was most effectively synthesized through the reaction of fatty acid ester and free fatty acids with 1,2-O-isopropyliden glycerol. The use of specific lipase enzyme (sn-1,3) highly likely result in the production of 2-monoacylglycerol from pure triacylglycerol or directly from natural vegetable oils and fats through alcoholysis reaction.

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