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Current developments in esterification reaction: A review on process and parameters

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ABSTRACT

Esters are among the highest volume of industrial organic compounds produced. They are frequently employed in various domestic and industrial processes. Fischer esterification regarded as the most common and widely practiced process of ester synthesis, faces serious limitations of low conversion and high reaction time attributed largely to establishment of equilibrium. Ester hydrolysis, reverse reaction to esterification, starts by supply of a byproduct- water. Several approaches have been developed to avoid equilibrium establishment and to improve overall conversion and rate of reaction, a significant difference exists between the current industrial practices and optimum esterification process/conditions. In the current review, a critical analysis of esterification techniques is conducted. Catalytic, non-catalytic thermal esterification, enzymatic esterification, along with factors affecting their productivity are discussed in detail. The current barriers, future challenges and potential of the esterification technologies are analyzed. Based on the comprehensive-data analysis, a novel technology-based solution is proposed.
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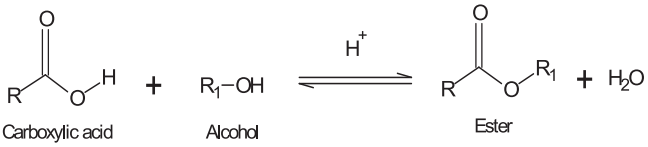
Introduction

Esterification is one of the most significant reactions in organic synthesis. The esters are found everywhere both as natural and synthetic organic compounds [1]. The major examples of esterification products are biofuels such as biodiesel [2,3], solvents such as ethyl acetate and methyl acetate [4], paints and varnishes [5], pharmaceuticals [6], plastics and coatings [7,8], and some are used as herbicides and pesticides[9,10]. Esters are frequently employed as flavoring components [11] and preservatives in food products [12], as important perfume additives [13], in soap and cosmetic industry as fragrances [14] or in personal care product formulations [15].

Typical Fisher esterification reaction involves heating a mixture of carboxylic acids and an excess amount of corresponding alcohols in the presence of a catalyst as shown in Eq. (1). The reaction achieves equilibrium after a certain time -- governed by process kinetics and thermodynamics. It requires addition of an excess amount of one reactant, usually alcohol, or the continuous removal of water to shift the equilibrium in the forward direction [16]. The reaction fails to achieve completion ultimately compromising the product yield.



(1)

The reaction is limited by slow rate of reaction and a low overall conversion owing to the establishment of thermodynamic equilibrium. Despite being commercially so important, the esterification process has yet to overcome these barriers in a cost effective and environmentally friendly way. Puterbaugh et al. reported ester yields between 58–75% after 1–4 hours of reaction by using variety of alcohols and acids under conventional reflux conditions [17]. In case of fatty methyl ester (FAME) production under conventional conditions, 65% conversion of FAME after 100 min of reaction is reported by Bakar et al. [18]; another study shows 78% conversion of methyl oleate within 60 min of reaction [19]. Similarly for com-

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mon solvents, 69% conversion of methyl acetate is achieved at 40 °C in a reaction carried out in a batch reactor without product condensation [20] also; 65% yield of ethyl acetate is obtained in a simple esterification reaction carried out using sulfuric acid at room temperature [21].

Synthesis of esters involves acylation of different alcohols with a variety of acid compounds such as carboxylic acids, acid chlorides, acid anhydrides, and lower esters. Acid chlorides, despite being the most commonly employed acylating reagents, are sensitive to moisture, have lower commercial availability and high reactivity that causes the acylation reaction sometimes to yield a complicated mixture of products [22]. Acid anhydrides exhibit similar chemical properties as acyl chlorides, therefore these two reagents are not always the best choice for forming esters. The reaction between carboxylic acids and alcohols is a condensation reaction, requiring stoichiometric amounts of the condensation reagents and continuous dehydration.

In order for the reaction to proceed forward and to make up for the low reactivity of carboxylic acids, suitable organic or inorganic catalysts are employed to assist accelerating the reaction while producing a diverse collection of ester compounds available. The ability of this reaction to perform under neutral conditions, while keeping different kinds of acid or base-sensitive functionalities intact, highlights its desirability and advantages over the other two reaction routes involving acid chlorides and acid anhydrides [16].

Significant research has been carried out in the field of catalysis [23–25], process design [26–29], and reactive distillation (RD) [30–32] to enhance the conversion and rate of reaction. However, there still exits a significant gap between current industrial practices and the optimum solution. In the conventional esterification process, there are several factors limiting the conversion and rate of reaction such as poor miscibility of reactants, inherent slow kinetics and accumulation of by product (water) bringing the system to a dynamic halt. Poor interaction between the reactants creates a thin film between the reactants, thereby limiting the mass transfer. The mass transfer can be enhanced by reducing the film thickness and shifting the equilibrium in forward direction by simultaneous removal of a byproduct. This is usually achieved by shear mixing or agitation, carrying out reaction under high temperature, pressure, supercritical conditions, or ultra-sonication, etc. These methods, though highly efficient, are cost-intensive and require high energy, making them uneconomical. To enhance the rate of reaction and overall conversion economically, microbubble mediated esterification has been introduced and investigated recently. It involves the use of a bubble reactor to produce microbubbles with higher surface energy and surface to volume ratio, higher internal pressure and surface temperature of bubble, providing larger interfacial areas, increased mass transfer and hence increased rate of reaction and overall rate of reaction [19]. Le-Chatelier's principle has been proposed to shift the equilibrium of the esterification reaction in forward direction as shown in Fig. 1. Alcohol is vaporized and fed in the form of microbubbles. The alcohols bubbles, as rise through the column, react with freshly available organic acids, in this case free fatty acids (FFA). The concentration gradient, present at all times, increases the mass transfer. The amount of alcohol present at the bubble surface is in excess relative to the FFA hence shifting the reaction towards the forward direction. Simultaneous removal of a by-product, water, pulls the equilibrium in the forward direction simultaneously.

In order to overcome the aforementioned challenges facing esterification reactions, it is of utmost importance to analyze the current status of esterification technologies, their challenges and future perspective and simultaneously identify emerging technologies with potential solutions. This review describes in detail the inherent chemistry and kinetics of the esterification reaction; its different types, what factors are considered while optimizing the process to obtain maximum efficiency along with different variables affecting its productivity. The properties and role of enzyme and different acid catalysts in accelerating the reaction rate has been discussed along with their associated advantages and disadvantages. Critical analysis of the status of the current technologies has been carried out along with their respective challenges. Potential of various techniques has been discussed to estimate their feasibility and applicability for large scale manufacturing. Based on review of the literature and recent lab experiments, a novel solution is proposed to enhance the rate of reaction and overall conversion of the esterification reaction. The purpose of this review is to understand the esterification process in detail and to thoroughly analyze different technical options available for improving product yield. Consequently, narrowing down to a solution that is sustainable, offers environmental benefits and bears answers to the pertaining challenges associated with esterification.

Non-catalytic thermal esterification

In order to save the catalyst manufacturing, recycling and disposal cost, several non-catalytic methods have been developed. Non-catalytic processes in esterification are also termed as thermal processes in which reactions are carried out at high temperature and high pressure without the use of a catalyst. In non-catalytic thermal esterification alcohol is heated to its subcritical or supercritical temperature that ensures fast reactivity between the reaction components at elevated temperatures. This procedure eliminates the need of a catalyst as, the purpose of lowering activation energy for effective collisions between reactant molecules is fulfilled by high temperature sub/supercritical alcohol instead of a catalyst. The term "thermal" in non-catalytic thermal esterification signifies high temperature conditions within the reaction mixture.

Non catalytic thermal esterification uses alcohol in supercritical/subcritical state. Supercritical fluids exhibit physical properties pertaining to both liquids and gases with densities and solvation capacities being similar to liquids and diffusivity equivalent to gases [33]. Fatty acid methyl esters (FAMEs) produced by this method are considered a green alternative to the conventional method as they do not involve use of additional chemicals [34]. Green synthesis of esters can either be carried out using enzymes as catalysts at lower temperature [35] or without the use of catalyst at higher temperature [36]. Esterification reaction performed using supercritical alcohol, e.g. supercritical methanol with critical temperature 512.5 K and pressure 8.084 MPa respectively, corresponds to high reaction rates giving complete conversions in a few min without the addition of an external catalyst at much higher temperatures, usually beyond 523 K [37].

In this method the dielectric value of alcohol e.g. methanol is lowered by heating to supercritical temperature so that only a single phase mixture of reactants is obtained instead of two phase oil/alcohol mixture. Since methanol is a polar solvent with hydrogen bonding, its hydrophobicity is enhanced by lowering dielectric constant under supercritical conditions [38]. Supercritical temperatures allow considerable yield of esters to be obtained as high temperature enhances the solubility between the reactants which in turn increases the reactivity and rate of reaction [39]. Critical temperature of methanol is 239.3 °C (512.45 K) therefore, for experiments conducted using methanol the temperatures are usually maintained between 280–320 °C to achieve supercritical state of methanol [40]. A comparison of some supercritical/subcritical esterification reactions is shown in Table 1. However, maintaining supercritical conditions with high operation temperature (523 K–673 K) and high pressure (10–25 MPa) makes this process extre-

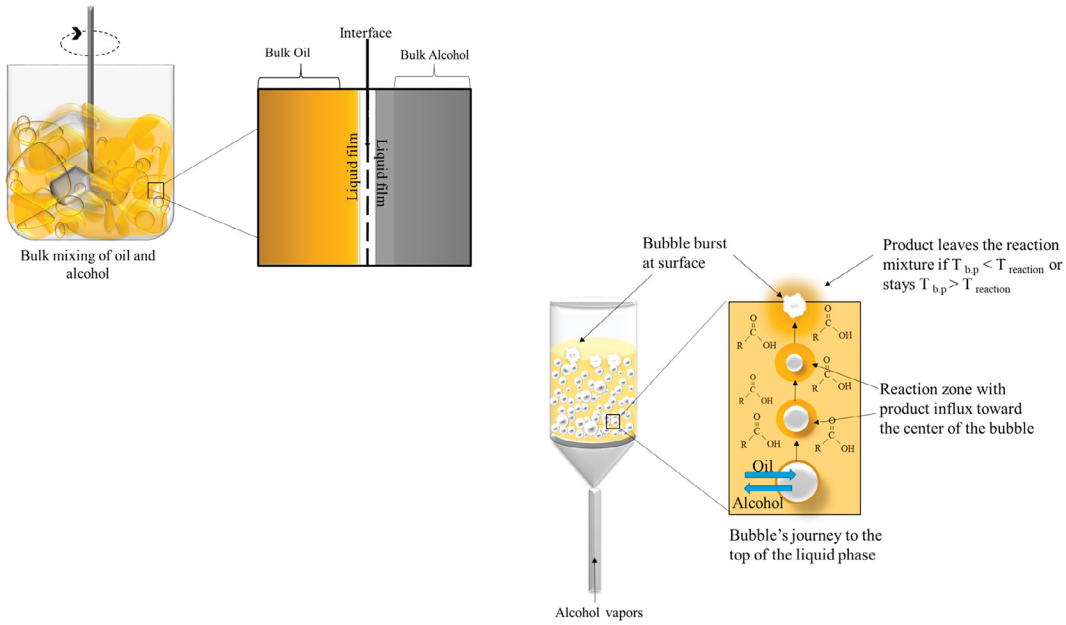

Fig. 1. Microbubble mediated esterification process.

Table 1
Esterification reactions performed under supercritical/subcritical conditions.

Reactants	Molar ratio Alcohol/Acid	Temperature (°C)	Pressure (MPa)	Reaction time (min)	Conversion (%)	Ref
Ethanol Levulinic acid	9:1	280	10	15	≤80	[43]
Methanol Sebacic acid	5:1	350	20	25	87	[44]
Methanol Rapeseed oil	0.9:1	270	20	30	94	[45]
Ethanol Waste oil/Crambe oil (25/75) blend	2:1	300	20	30	~70	[39]
Methanol Rapeseed oil	14:1	270	17	15	97	[46]
Ethanol Mixture of distillate fatty acids (MDFA)	6:1	280	10	10	90	[47]

mely energy intensive. Use of high temperature and pressure, extensive safety measures and costly reactor units increase the principle cost of the process significantly [36,41,42].

Catalyzed esterification reactions

Absence of a catalyst reduces the rate of reaction significantly. A suitable catalyst is, therefore, inevitably required. An ideal catalyst provides high catalytic activity, enhanced kinetics, handling facility, minimal waste production, separability from the final product mixture, and recyclability [48]. Russo et al. studied reaction kinetics of nonanoic acid esterification with 2-ethylhexanol in a batch reactor. Blank tests performed without a catalyst gave 5% yield after the experiment was allowed to run for 5 h whereas sulfuric acid catalyzed reaction provided more than 80% yield within 2 h of reaction [49]. Mandake et al. carried out a study on catalyzed and auto-catalyzed esterification reaction in a batch stirred reactor to observe reaction kinetics between acetic acid and ethanol. Results from the study showed 14% conversion achieved for non-catalyzed reaction compared with 54% achieved in catalyzed reaction after 180 min [50]. Mendes de Paiva et al. performed a comparative study involving catalytic and non-catalytic production of ethyl laurate under high temperature (180 °C). The results obtained showed conversion of around 80% in case of non-catalyzed reaction in 120 min, while the reaction performed using ZnL_2 catalyst provided 92% conversion at same temperature after 110 min [51]. Santaella et al. reported 20% conversion after 1000 min in reaction between acetic acid and ethanol under non catalytic conditions using RD column [52]. 1% conversion of salicylic acid and methanol to methyl salicylate was obtained when refluxed for 20 min at 105 °C under microwave irradiation in the absence of a catalyst [53]. It may take several days for the reaction to provide even limited conversions, due to the reversibility and low reaction rates. Hence, in order to boost productivity and make the reaction proceed faster to obtain desired yield in shorter period of time, use of catalyst is considered essential.

Acid catalyst acts as a proton donor to the carboxylic acid making it labile for a quick nucleophilic attack by alcohol. The activity of a catalyst can further be enhanced by varying the reaction conditions like temperature, using alcohol in excess or combining the catalyst with activator/promotor [54,55]. Mechanism of esterification catalyzed by sulfuric acid is provided in the supplementary material from Eqs. S1-S6. In the first step, acetic acid receives a proton from sulfuric acid which attaches itself to the oxygen via the lone pair. The transfer of H^+ to oxygen creates a positive charge that is delocalized. Subsequently, the lone pair on the oxygen atom of ethanol attacks the positively charged carbon of acetic acid. In the next step, a water molecule leaves, hydrogen sulfate reclaims the proton yielding the ester product, and sulfuric acid is regenerated. The most widely employed catalysts for esterification are the traditional homogeneous catalysts such as sulfuric and hydrochlo-

ric acids and heterogeneous catalysts such as ion exchange resins [56]. In the subsequent section, a critical analysis of homogeneous and heterogeneous catalysts is carried out.

Homogeneous acid-catalyzed esterification

Homogeneous acid catalysis (liquid–liquid phase) is one of the most popular commercial esterification techniques. H_2SO_4, HCl, HI and p-toluene sulfonic acid are mostly widely used catalysts. A detailed analysis on the use of several homogeneous catalysts under different experimental conditions and corresponding reaction time and yield of the reaction is given in Table 2. Among these mineral acids, H_2SO_4 finds the most extensive application as a BrØnsted acid. It is strongly acidic and a powerful dehydrating agent. This strong acidity offers the protonation of carboxylic acid by the release of H^+ ions in higher concentration at a very fast rate. Several studies suggest that sulfuric acid is responsible for greater catalytic action than heterogeneous catalysts in providing enhanced conversions Jyoti et al. analyzed performance of various acidic catalysts for ethyl acetate production. Sulfuric acid has been reported to perform better than other homogeneous and heterogeneous catalysts giving 63.2% conversion compared to 61.02%, 53.3%, 21.4%, 34.96%, and 14.84% obtained for p-TSA, HCl, HI, Dowex 50WX, and Amberlyst 15 respectively [56]. The use of homogeneous catalysts provides better availability of free protons in liquid–liquid reaction mixtures, resulting in faster rates of reaction relative to the systems in which heterogeneous (liquid–solid reaction mixture) are used [54,57]. In cases where the acidity of a compound is not strong enough to trigger the desired action, the acid is either combined with an activator or reaction conditions are modified to accelerate the reaction, as in case of microwave irradiation or ultrasound to accelerate these intrinsically time consuming reactions [58]. Homogeneously catalyzed reactions under microwave irradiation finish reactions that usually last for multiple hours within a few min with commendable yields [59]. Microwave irradiated esterification using a conventional setup using *p*-toluene sulfonic acid (PTSA) catalyst was studied by "Nagahata et al. for the production of amino acid esters. A yield of 63.7% of L-leucine butyl ester after 30 min using conventional heating as compared with 100% yield achieved after 10 min of reaction carried out under microwave irradiation [60]. Yan et al. used ultrasonic-microwave combined intensification for esterification with an ionic liquid catalyst revealing 97.85% conversion after 15 min compared to the same conversion obtained using conventional method within 180 min [61]. However, in terms of environmental risk, generation of large amounts of toxic waste, handling, specialized materials and higher cost of separation and product purification are the major challenges of homogeneous acid catalysis [62].

Mineral acid reagents are highly corrosive and requires specialized material not only for process equipment but for pipe and fittings etc., as well. These compounds require careful handling as they are hazardous and can affect personal safety. Acid catalysts such as H_2SO_4, HF, $AlCl_3$ and BF_3 lead to process difficulties because they are soluble in a wide range of organic reaction medium or exist as a separate layer. Post reaction, these catalysts need to be separated. It requires additional use of alkali for neutralization thereby consuming additional resources and increasing process cost. The volume of toxic waste produced typically exceeds the product volume, causes separation problems and is environmentally undesirable. Its unchecked release into the environment can result in unwanted pollution. Furthermore, the waste disposal costs are sometimes higher than the original cost of the raw material required for processing [63].

Heterogeneous acid-catalyzed esterification

Homogeneous catalysts such as mineral acids are inexpensive and provide high conversion. However, as discussed above, they make downstream separation complex by generating byproducts during neutralization, are environmentally toxic and difficult to handle. To counteract these problems, solid acid catalysts (SACs) were considered as a substitute to liquid acid catalysts. SACs are generally produced by attaching acid functional groups to solid support via physical or chemical method generating catalysts with available active sites for fast reactivity [73]. Heterogeneous acid catalysts such as zeolites [74,75], heteropolyacids [76,77], ion-exchange resins [78,79], supported chlorides [80,81] are being widely researched as an environment friendly option to make the

Table 2
List of homogeneous acid catalysts with optimum conditions for esterification.

Reactants	Molar ratio Alcohol/ Oil	Catalyst	Catalyst conc. (Wt. %)	Temperature (°C)	Reaction time (min)	Yield %	Product	Experiment setup	Ref
Oleic acidOleyl alcohol	1:1	H_2SO_4 Perchloric acid Phosphoric acid	1.25	90	300	93.88 54.9 52.7	Oleyl oleate	Oil bath stirring	[64]
Acrylic acid Ethanol	1:1	H_2SO_4	3	70	360	83.99	Ethyl acrylate	Batch reactor	[54]
Naphthenic acids Methanol	14:1	H_2SO_4	0.7	80	360	95	Methyl naphthenate	Batch reactor	[65]
Oleic acid 1-octanol	1:1	DBSA (dodecylbenzene sulfonic acid)	5	23	1440	98.7	Octyl oleate	Dean Stark apparatus	[66]
C. minutissima microbial oil Methanol	9:1	H_2SO_4	3	80	480	>96	FAME	Closed glass reactor	[67]
Ferulic acid Ethanol	6:1	H_2SO_4	10	75	3	95	Ethyl ferulate	Microwave Irradiation	[59]
Tall Oil Fatty Acid Methanol	15:1	H_2SO_4	0.5	55	60	96.76	FAME	Dean Stark appratus	[68]
Citric acid Ethanol	7:1	Methanesulfonic acid	2	119	20	91	Triethyl citrate	Batch reactor	[69]
FFA Methanol	15:1	BF3	5.33	Ambient	15	100	FAME	Ultrasonic	[70]
Acetic acid Ethanol	1:1	Ionic Liquid (1-(4-sulfonic acid) butylpyridinium hydrogen sulfate)	0.2	100	240	>99	Ethyl acetate	Oil bath stirring	[71]
Palm fatty acid distillate (PFAD) Methanol	1.5:1	H_2SO_4	7.3	120	70	99.34	FAME	Dean stark apparatus	[72]

process of esterification green. These catalysts are however, non-renewable therefore a new trend is on the rise for production of carbon based renewable Solid Acid Catalysts (SACs). SACs have their carbon supports sourced from renewable material. Acid functional groups are, subsequently, attached via covalent bonding with carbon atoms [73]. Reported use of different sulfonated carbon based solid catalysts for the process of esterification bearing excellent yields include powdered coal based acid catalyst [82], rice husk, moringa oleifera seeds, and lipid extracted marine algae carbon biomass catalyst [83], sulfonated functionalization of murumuru kernel shell [84], corn cob residue [85], sunflower shells [86], monk fruit seeds [87] and magnetic biochar catalyst derived via palm oil biomass from empty fruit bunches [88]. Use of sludge from wastewater treatment plants as heterogeneous catalysts after acid treatment has recently been reported by Junior et al. to provide more than 90% yield for biofuel production [89]. Heterogeneous acid catalysts have been reported to provide significantly higher yields as compared with homogeneous catalysts. Mya et al. demonstrated a study with zeolite catalyst ZSM-5 offering high esterification rate comparable to sulfuric acid. The study proposes zeolite catalyst ZSM-5 as an alternative of sulfuric acid due to its reduced corrosive properties [90]. Similar results of higher yields of 90.4% and 89.97% achieved for sulfuric acid and sulfated alumina respectively have been reported by Ulfah et al. [91]. Carrying out esterification in the liquid phase using heterogeneous cation exchange resins has the advantage of lower separation cost with potential usage in continuous and micro reactors [92,93] with simplified reaction configurations. A detailed analysis on the use of several heterogeneous catalysts under different experimental conditions with corresponding reaction time and yield of the reaction is given in Table 3.

Several heterogeneous catalysts involve silica gel support as the structure provides impressive chemical and thermal stability, large surface area and better solid acidic site accessibility. One of the examples includes sulfonic acid-functionalized silica which is a nano porous solid acid catalyst with easy synthesis and use in esterification process [62]. Sulfonated hyper cross-linked polystyrene resin, sulfonated polyvinyl alcohol and sulfated zirconia for transesterification and esterification of free fatty acids for biodiesel production using oleic acid with different alcohols [94–96].

Solid acid catalysis despite offering some prominent advantages of environmental friendliness, lower separation cost and recyclability [63,97] over liquid acid catalysis comes with certain drawbacks. Most popular heterogeneous acid catalysts employed for esterification such as zeolites, Amberlyst-15, ion exchange resins and silica supported heteropolyacids have limited mass transfer. They are often expensive and give low product yields. Wu et al. investigated the catalytic behavior of homogeneous sulfuric acid catalyst and heterogeneous Amberlyst-70 in bio-oil's acid treatment with methanol. Based upon results, that showed better performance of sulfuric acid compared with Amberlyst-70, was proposed to be carried out via hydrogen ion dispersion in reaction medium. Hydrogen ions from sulfuric acid were uniformly dispersed in entire mixture which facilitated the reaction whereas Amberlyst-70 hydrogen ions remained locally concentrated. Heavier organic acid molecules also found it difficult to access acid active sites in catalyst pores due to steric hindrance ultimately contributing to low conversion [98]. Zeolites have low thermal stability for cation exchange resins such as Amberlyst-15 (<140 °C) and loss of active acid sites in the presence of polar medium [99]. The regeneration of catalyst, exchange after intervals and losing heat resistance with time are some barriers are also some drawbacks of heterogeneous catalysts. [100].

However, research is still underway to create catalysts for esterification that are inexpensive and offer environmental benefits in terms of low cost and ecofriendly design.

Enzymatic esterification

Enzymes used in reversible reactions like all other catalysts affect the rate of reaction in both directions, the direction taken, however, is determined by thermodynamics. Equilibrium limited reactions catalyzed by enzymes such as hydrolases require altering the concentration of one of the reaction components, mainly water, to displace equilibrium. Decreasing concentration or suppressing the activity of water by its extraction from the system in a reversible reaction can theoretically make any hydrolase catalyze the corresponding reaction towards the synthesis of desired product. Lipase and esterase, belonging to the hydrolase class, are among the most widely discussed enzymes in studies dealing with enzymatic action [111]. A detailed analysis on the use of several homogeneous catalysts under different experimental conditions and corresponding reaction time and yield of the reaction is given in Table 4.

Lipases (triacylglycerol ester hydrolase; EC 3.1.1.3) are biocatalytic enzymes which can work under unfavorable conditions pertaining to their high stability [112]. They are known to catalyze wide variety of reactions that include hydrolysis, interesterification, esterification, transesterification, alcoholysis etc. [113]. Enzymatic catalysis is being widely studied for biodiesel production using novel methods for enhancing efficacy of the process [114–116]. Wancura et al. reported production of biodiesel from waste cooking oil using lipase enzyme (Eversa® Transform 2.0.) giving 96.2% FAME yield at 40 °C for useful transformation of waste into energy [117]. The physiological role of lipases is to catalyze the conversion of triglycerides into mono or di-glycerides, fatty acids and glycerol. Eqs. S7-S10 in supplementary material provide mechanism for lipase catalyzed esterification involving formation of two tetrahedral intermediates in step 1 and 3. The reaction intermediate in step 3 releases the ester molecule to return the enzyme to its native form. Different lipases perform different actions specific to their own type, i.e. some are capable of hydrolyzing the primary and secondary esters while others can only hydrolyze primary ones. Some groups can perform bond cleavage of particular fatty acid types only [26]. The path followed by a lipase in a chemical reaction is highly dependent upon the water content of the system -- absence of water in a reaction media can diminish the competing hydrolysis reaction. There are several studies available that report enzyme assisted catalysis in systems that are either water free (non-aqueous) or have low water content [118].

Lipases catalyze esterification and transesterification reactions in organic solvents and other non-aqueous media like supercritical fluids. In case of reversible reactions like esterification, enzyme-assisted catalysis carried out in organic solvent media is favorable as it forces the thermodynamic equilibrium towards ester formation. Improvement in activity of lipases in water free systems has been studied by employing various techniques like immobilization on insoluble supports (e.g. polymers), reverse micelles, entrapment in micro emulsions, non-covalent interaction with surfactants and a few others [119].

The enzyme instability under harsh conditions can be improved by immobilizing them on a solid support. It allows reduced consumption of the catalyst for it to be retrieved and reused for multiple repeated reaction cycles [120,121]. It also helps provide better resistance to avoid changes in performance or loss of activity during the reaction by providing prolonged stability and availability of wider options for reactor design [122]. Water generation plays a key role in establishing equilibrium in esterification reactions. Mass transfer problems that arise due to the presence of large quantities of undissolved alcohol in bulk esterification reactions can be avoided by using immobilized lipase enzymes. Enzyme immobilization aids in enhanced dissolution of alcohol in the system. This ultimately beneficially forces the available organic acid to

Table 3
Different heterogeneous catalysts used for acid catalyzed esterification.

Reactants	Molar ratio Alcohol/ Acid	Catalyst	Catalyst conc. %	Temperature (^{0}C)	Reaction time (min)	Yield (%)	Product	Catalyst reusability, Runs/ Activity loss, %	Experiment setup	Ref
Oleic acid n-Butanol	1:1.2	$Zr(SO_4)_2$. $4H_2O$	5	120	480	94.5	Butyl oleate	5/15	Dean Stark apparatus	[101]
Oleic acid Methanol	5:1	SLO/HZSM-5 (HZSM-5 impregnated with sulfated lanthanum oxide (SO4 2/La2O3))	10	100	420	100	Methyl oleate	3/50	Batch reactor with constant agitation	[102]
Oleic acid Methanol	9:1	Sulphonated carbon-based waste ginger straw	7	64	210	93.2	Methyl oleate	5/28	Dean Stark apparatus	[103]
Oleic acid Methanol	9:1	WO3/ZrO2	20	75	120	93	Methyl oleate	–	Autoclave batch reactor	[104]
Oleic acid Methanol	18:1	SO_3H-HM-ZSM-5–3	5.2	88	600	100	Methyl oleate	–	Dean Stark apparatus	[105]
Acetic acid Isoamyl alcohol	1.1:1	$Cu(CH_3SO_3)_2{\cdot}4H_2O$ (Copper(II) Methanesulfonate)	0.25	110 ~ 115	120	96	Isoamyl acetate	5/negl	Dean Stark apparatus	[106]
Acetic acid n-hexanol	1:1	Sulfonic acid-functionalized MIL-101	0.05	110	300	65.1 99*	Hexyl acetate	5/negl	Dean Stark apparatus	[107]
Oleic acid Methanol	3:1	Amberlyst-46	15	100	120	98.6	Methyl oleate	10/>2	Dean Stark apparatus	[108]
FFA Methanol	12:1	Acid-modified Montmorillonite (k10) clay	6	55	120	80.8	FAME	3/28	Hot plate with magnetic stirrer and reflux condenser	[109]
Oleic acid Methanol	15:1	Sulfonated *Sargassum horneri* carbon	10	70	180	96.4	Methyl oleate	4/neg	Three-mouth flask in an oil bath	[110]

react completely towards ester synthesis as shown in Fig. 2. It serves as a substitute to removing the water produced during reaction, maintaining minimal water levels to avoid simultaneous hydrolysis of the produced ester [123]. Despite some considerable benefits commercial immobilization of lipases, it is considered an expensive method because of high cost for support material and complexity of enzyme immobilization process. Cost effectiveness of this process is also undermined considering gradual loss of catalytic activity after each repeated cycle. The reaction byproduct glycerol being oil insoluble adsorbs on the surface of immobilized enzyme thereby suppressing its activity and causes loss of operational stability [124]. Therefore, to bring down the cost of utilization of enzyme catalyst researchers are studying enzymatic hydroesterification as cost effective alternative in which enzymes are used as soluble/liquid formulations [125–127]. Another cheap alternative in the form of Dry Fermented Solids (DFS) has been proposed recently. It involves cultivating lipases in solid-state fermentation and then those solids are dried to be added directly into the reaction mixture for accelerating the reaction. This process avoids the need to immobilize the lipases on solid matrix after recovering from a fermented liquid broth [128].

Another option to improve productivity is to use alcohol in large excess along with simultaneous removal of byproduct water in order to push the reaction forward. However, a balanced choice of lipase and anhydrous alcohol is required before starting the reaction as using an excess amount of alcohol can cause enzyme deactivation [123,129]. Enzyme inhibition by the most commonly used alcohols in esterification reactions i.e. methanol and ethanol has been reported in literature [112,123]. For enzymatic esterification, rate of reaction increases with increase in concentration of the substrate up to a certain limit. Increasing the concentration beyond a particular limit decreases the rate of reaction due to the inhibitory effect of alcohol on enzyme catalyst. The immediate reaction between alcohol and enzyme causes the alcohol to block the nucleophilic site on enzyme, engaged in acylation process, thus suppressing the enzyme's reactivity. Inhibitory effect is strongly manifested by primary alcohols due to the smaller size of alcohol moiety. Reactivity and corresponding inhibition is lower for secondary and tertiary alcohols due to the steric effect or increased bulkiness of the alcohol molecule [130]. In another study performed by Staudt et al. authors described the reason behind enzyme inhibition by excess alcohol in the system as alcohol's interaction with lipase by hydrophobic-hydrophilic forces. Alcohol's bipolar structure with a hydrophilic head and hydrophobic tail allows greater contact time between lipase and alcohol that causes water layer displacement around biocatalyst leading to its partial dehydration. Change in native conformation caused by water loss leads to enzyme inhibition [131].

Two major drawbacks are associated with conventional bio catalysis: (i) high cost of enzymes and (ii) mass transfer limitations resulting in low conversions [111]. The use of organic solvents to support ester formation and purification in enzymatic esterification is an obstacle to making the process green and environmental friendly [15]. Maintaining the mechanical stability of the enzyme and continuous removal of water are two major obstacles to scaling up this method for industrial applications [112]. Also enzyme immobilization is reported to provide lower conversions as compared to free enzymes due to the inefficient enzyme-substrate interaction [122].

Non-catalyzed or auto-catalyzed esterification is regarded as a green substitute to chemically catalyzed processes for it eliminates the need of separation and neutralization processes commonly required in catalyzed reactions for product purification. Elimination of these steps from manufacturing phase saves significant amount of time and money. Also, autocatalysis is usually performed under extreme conditions that allows fast reactivity and

Table 4
Different enzyme catalysts utilized for esterification.

Reactants	Molar ratio Alcohol/ Acid	Catalyst	Catalyst conc. %	Temp., °C	Reaction time, min	Yield (%)	Product	Experiment setup	Ref
Oleic acid Stigmasterol	3:1	*Candida rugosa* lipase	8	45	960	97.33	Stigmasteryl oleate	Stirred reaction vials	[132]
Oleic acid n-propanol	–	Immobilized lipase type B from *C. antarctica* (CALB; Novozym 435)	5	32	480	91.7	Propyl oleate	Erlenmeyer flasks on orbital shaker	[133]
Formic acid Phenethyl alcohol	5:1	Novozym 435	15	40	240	95.92	Phenethyl formate	Shaking incubator	[134]
Acetic acid Isoamyl alcohol	3:2	Novozym 435	0.6	50	240	98	Isoamyl acetate	Switchable ionic liquid/solid phases	[135]
Geraniol and Citronellol Cinnamic acid	3:1	Novozym 435	15	70	2880	99 98	Geranyl cinnamate Citronellyl cinnamate	–	[131]
Hexanol Formic acid	5:1	Novozym 435	15	40	90	95	Hexyl formate	Serum bottles in shaking incubator	[136]
Acetic anhydride Eugenol	5:1	Novozym 435	10	60	240	99	Eugenyl acetate	Erlenmeyer flasks on orbital shaker	[137]
Octanoic acid Hexanol	1:1	*Candida antarctica* lipase (Novozym 435)	–	35	60	90	Hexyl octanoate	Glass viles in thermoshaker (Batch reactions)	[138]
Propionic acid Geraniol	6:1	*Candida antarctica* lipase (Novozym 435)	5	40	30	100	Geranyl propionate	Erlenmeyer flasks on orbital shaker	[139]

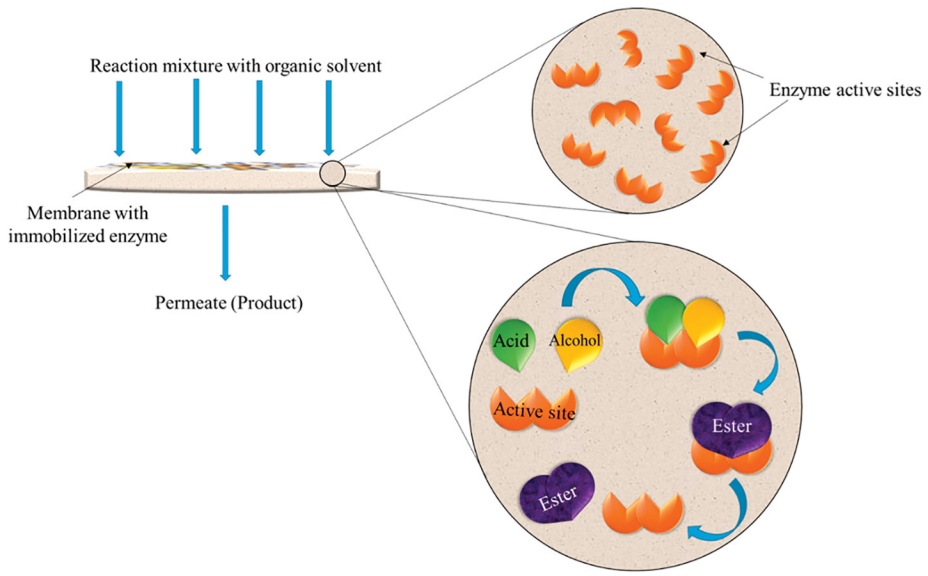

Fig. 2. Esterification via immobilized enzyme solid support catalyst.

desired yield is achieved in a relatively short period of time. But its energy intensiveness and elaborate safety measures with costly installation at large scale are some of the drawbacks that make the process uneconomical. Catalyzed esterification on the other hand is the most common technique utilized for large scale ester production. It offers low cost options with many choices easily available for best practices. Homogeneous catalysts uniformly disperse in the reaction medium and provide fast reaction rates but cause damage to plant parts and generate toxic waste that requires extensive treatment. Heterogeneous catalysts are environment friendly options with majority of new studies focused on affirming their high efficacy but, they are costly and some offer poor recyclability resulting in low profitability in exchange of high cost investment. Enzyme catalysis offers high selectivity and prevents the use of harmful chemicals often requiring mild conditions to work but they are sensitive to different reaction conditions ultimately leading to enzyme deactivation.

Trans-esterification reactions

Trans-esterification, also known as alcoholysis, is a reaction between an oil/fat and alcohol to produce ester and glycerol in the presence of catalyst that may be an acid, alkali or an enzyme [140] as shown in Eq. (2). Since the reaction is reversible, obtaining a high yield of esters demands the alcohol to be put in excess that aids in pushing the reaction in forward direction [141,142]. Methanol and ethanol are two commonly used alcohols in the trans-esterification process. Methanol however is preferred because it is cheap and has physical and chemical advantages of low boiling point, high reactivity due to short carbon chain, while inability to form azeotropes facilitates recovery [143]. Catalytic trans-esterification between oils and methanol has been extensively studied using either a homogenous or heterogeneous acid or base catalyst [95,144–146]. Alkali catalysts are most commonly employed for transesterification as they give fast reactivity using

small catalyst concentration under low temperature conditions in relatively short period of time, compared to acid catalysts. However, one common problem associated with their use is sensitivity of base catalysts to the presence of water or high FFA content of oil that can lead to soap formation with subsequent emulsification [147].

Homogeneous acid catalysts for transesterification include sulfuric acid, sulfonic acid or hydrochloric acid while homogeneous base catalysts involve sodium hydroxide, potassium hydroxide, sodium methoxide as alkaline liquids as shown in Table 5. Heterogeneous catalysts are solid acid and base, namely alkaline-earth metal compounds, titanium-silicates, anion exchange resins and immobilized enzymes as shown in Table 6 [148,149]. The use of heterogeneous catalysts is growing. However, the employment of traditional homogeneous catalysts is still quite common at industrial scale due to the lower costs, reduced mass transfer limitations and high catalytic activity [140,150].

Transesterification for the production of fatty acid alkyl esters has several advantages but there are a few drawbacks such as high processing time of transesterification of vegetable oils and the post treatment procedures required for the purification of product, e.g. separation, neutralization, water washing and heating in case of using homogeneous acid/base catalysts [151,152]. Heterogeneous base catalysts, on the other hand, though cost-effective, require relatively high temperature to promote reactivity compared to their homogeneous counterparts. Furthermore, the problem of possible catalyst leaching has raised environmental concerns [147]. Saponification resulting from high FFA content of the feedstock results in consumption of catalyst, an incomplete reaction with formation of an emulsion, rendering separation of glycerol difficult [153,154]. Prevention of soap formation by using a two-step transesterification approach, with preliminary esterification treatment of high FFA content utilizing an acid catalyst, can solve this problem but comes with additional cost of instrumentation and operation [155]. Among enzyme catalysts lipases is most commonly studied for catalyzing transesterification. Enzyme catalyst usage can provide benefit of skipping all the separation and purification processes, but inhibition of enzyme by high alcohol concentrations, longer reaction time, high cost and commercialization are some of the challenges associated with its infrequent use [147,155].

Factors affecting the esterification reaction

Reaction of carboxylic acids with alcohols in the presence of an acid catalyst in most cases corresponds to the union between alkoxy and acyl groups. There are several factors that affect the reaction chemistry of esterification.

Effect of structure of reactants

Structure of a molecule and types of functional groups or substitutes associated with carboxylic acids and alcohols determine the speed at which both reagents are esterified as well as the extent of equilibrium. Primary alcohols undergo quick and complete esterification in the formation of esters, i.e. methanol is known to provide maximum yield and fastest reaction. Ethyl, *n*-propyl, *n*-butyl: all three alcohols react with similar speed and conversions. Secondary alcohols under similar conditions react comparatively slower and give lower yields of ester products. Tertiary alcohol reactions are even slower and conversions ranging from 1 to 10% at equilibrium are achieved [181]. The decrease in reactivity in case of secondary and tertiary alcohols is due to steric hindrance (or bulkiness) on the hydroxyl group of alcohol by the neighboring molecular groups (Fig. 3). This hindrance reduces the surface area available for nucleophilic attack by the alcohol on carbonyl carbon of carboxylic acid thus affecting the rate of reaction [182] (attack shown in Eq. S3 in supplementary material).

Acetic, propionic, butyric (straight chain acids) along with phenylacetic and β-phenylpropionic acids are esterified conveniently with isobutyl alcohol at 155 °C. Highest initial rate of reaction is exhibited by formic acid. Presence of a branched chain in acids slows down the rate of reaction. Addition of more chains in acid structure further reduces the reaction rate. However, these substituent acids offer higher conversions in comparison to the normal straight chain acids. Aromatic acids like benzoic and *p*-toluic acid in the same manner react at a slow pace but provide high equilibrium conversions. Some of the factors that cause the reaction to proceed slowly include the introduction of nitrile group on aliphatic acids, increase in chlorination of chloracetic acids and presence of double bonds. Several studies have concluded that the α,β-unsaturated acids are esterified with difficulty compared to their saturated analogues. Similarly, the triple bond at alpha or beta sites on acids show such difficulty. However, β, γ-double bond displays lower resistance. Rates of reaction reduce significantly for conjugated double bonds at β, γ positions. Unsaturated acids with cis-substitution delay esterification in contrast to the transisomers [183]. Ethyl ester synthesis, utilizing anhydrous ethyl alcohol catalyzed by hydrogen chloride with straight chain fatty acids (propionic till stearic acid), shows the rate of esterification to be constant. Conversely, chain branching of the fatty acid causes retardation. Saturated dibasic acids esterify to a maximum rate at glutaric acid. Cycloparaffin monocarboxylic acids esterify with an increasing ease in the order C3, C7, C6, C5, and C4 rings excluding cyclo-

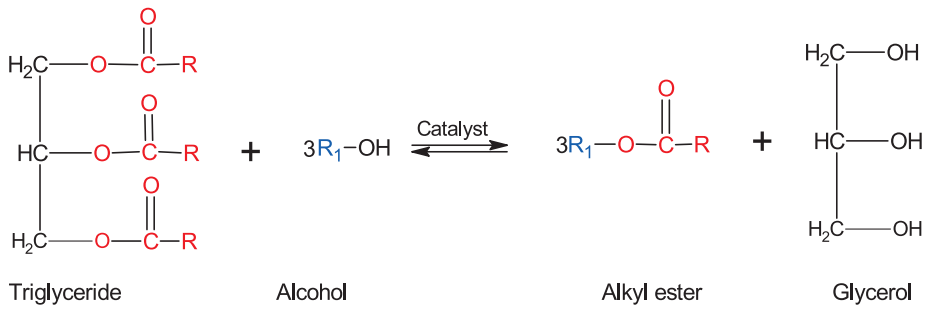

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Table 5
Various homogeneous catalysts employed for transesterification reactions.

Edible and Non-edible Oil	Molar ratio Alcohol/Oil	Catalyst	Catalyst conc. (wt. %)	Temperature (°C)	Reaction time (min)	Yield %	Ref
Soybean	6:1	NaOH	0.3	45	10–20	100	[156]
	10:1	$NaOCH_3$	0.5	75	30	94	[157]
Sunflower	6:1	KOH	1.3	25	60	98.4	[158]
	3.75:1	$NaOCH_3$	0.5	60	60	100	[159]
Cottonseed	6:1	KOH	0.6	55	60	96	[160]
	6:1	NaOH	1	60	120	90	[161]
Jatropha	6:1	KOH	1	50	120	97	[162]
	9:1	NaOH	0.8	45	30	96	[163]
	5.9:1	H_2SO_4	15	60	1440	99.8	[164]
Neem	8:1	H_2SO_4	0.08	15	50		
	8:1	NaOH	1	60	60	85	[165]
	6:1	KOH	1	65	40–50	96	[166]
Pongamia pinnata	6:1	H_2SO_4	2	65	300	89.8	[167]
	10:1	KOH	1	105	90	92	[168]
	9:1	NaOH	0.5	45	30	89.5	[169]

Table 6
Various heterogeneous catalysts employed for transesterification reactions.

Edible and Non-edible Oil	Molar ratio Alcohol/Oil	Catalyst	Catalyst conc. (wt. %)	Temperature (°C)	Reaction time, (min)	Yield (%)	Ref
Rapeseed	6:1	SO42−/ZrO2	6	200	60	95	[170]
	18:1	CaO/MgO	2	64.5	210	92	[171]
Palm kernel	8:1	Montmorillonite KSF	3	190	180	79.6	[172]
	12:1	Rice husk-derived sodium silicate	2.5	65	30	97	[173]
Soybean	30:1	Cs-Na_2ZrO_3	1	65	15	98.8	[174]
	2:1	Micro-structured calcium oxide from chicken egg shells	5	65	180	85.83	[175]
Jatropha	6:1	Sulphonated phenyl silane montmorillonite	5	50	150	98	[176]
	9:1	KOH/calcined waste animal bones	6	70 ± 3	180	96.10	[177]
	9:1	CaO/MgO doped with strontium	5	65	120	99.6	[178]
Castor	12:1	Iron (II) doped ZnO nanocatalyst	14	55	50	91	[179]
	14:1	Mud clam shell calcium oxide	3	60	120	96.7	[180]
	12:1	Sulphonated phenyl silane montmorillonite	5	60	300	89.8	[176]

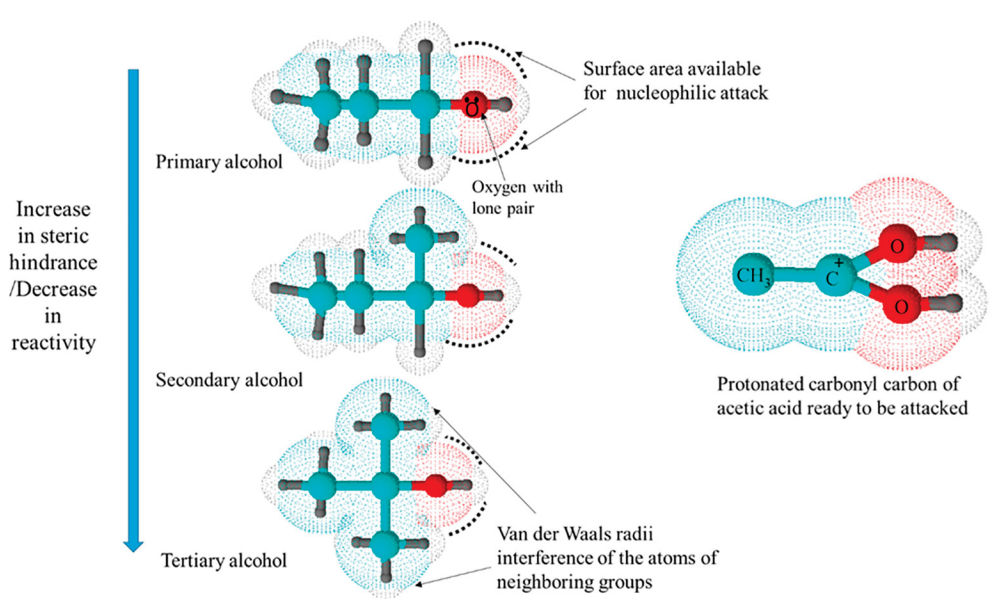


Fig. 3. Effect of neighboring groups on reactivity of subsequent alcohols in esterification.

propanecarboxylic acid. The reaction speed exhibited by these acids is greater than their open chain counterparts. Substitutions that cause electron displacement toward aromatic acid carboxyl group reduce the reaction rate [184]. Fluoromethoxy or ethoxy groups' substitution at *ortho* position of the ring displays accelerating action, while bromo, iodo, methyl and nitro groups decelerate. The activity of groups in the *meta* and *para* position is not well known [185].

Kinetic considerations

Kinetic principles applied to industrial reactions are often quite useful. Initial studies related to the kinetic considerations of an esterification reaction are performed at a small level in a well stirred batch reactor. In several cases batch study results provide considerable evidence for the evaluation of esterification reaction performance in a continuous operating system. The temperature effect on reaction rate is given by the Arrhenius equation. In case of acid catalysis rate of esterification reaction corresponds to the acid or hydrogen ion concentration, alcohol and carboxylic acid concentration. All these factors related to each other can be used to estimate the optimum required operational condition. The order of the reaction, mathematical equation describing production rate with time, quantity of the catalyst, empirical equation representing the reaction rate constant relation with temperature and reactant proportions are the important parameters.

In esterification reaction, equilibrium is responsible for the limiting conversion of the reactants Eq. (3). Equilibrium constant (K_{eq}) of esterification reactions have values ~1 ~ 10 representing presence of considerable amounts of reactants in equilibrium mixture. Smaller the value of K_{eq} greater will be the concentration of reactants present at equilibrium and vice versa as can be seen from Eq. (4). To make the reaction move towards product formation equilibrium displacement is carried out by continuous withdrawal of one of the product – especially water – from the reaction mixture via distillation [186].

$$A + B \underset{K_r}{\overset{K_r}{\rightleftharpoons}} C + D \tag{3}$$

$$k_{eq} = \frac{[C_c]_{eq}[C_D]_{eq}}{[C_A]_{eq}[C_B]_{eq}} \frac{k_f}{k_r} \tag{4}$$

Bimolecular Fischer esterification reaction involve five elementary reactions that make up the whole ester formation mechanism i.e. formation of protonated carbonyl substrate, attack of nucleophile to produce tetrahedral intermediate, OH group conversion into a good leaving group, loss of a water molecule and finally loss of a proton giving the ester product. Esterification of primary and secondary alcohols follow the same mechanism usually. The structure of corresponding acid and alcohol determines the rate of reaction, straight-chain structure is easier to esterify than branched-chain structure and the rate declines with increase in chain branching [145].

The role of catalyst in reaction mechanism addresses the need to control the reaction at molecular level [187]. Use of a catalyst in a reversible reaction does not change the position of equilibrium rather it changes the amount of energy needed to attain the same position of equilibrium in both forward and backward reactions. Several mechanisms have been proposed for both heterogeneous and homogeneous catalyzed esterification reactions [188–193] and multiple kinetic models such as power-law model, the pseudo-homogeneous model, the L-H model, the E-R model have been developed to understand the kinetic behavior of esterification reactions [145]. Many experimental studies have been carried out to understand the mineral acid promoted kinetics of esterification [188–196]. Mekala and Goli performed simple bimolecular reaction between methanol and acetic acid with sulfuric acid as a catalyst at different temperatures, catalyst concentrations and feed molar ratios in a well stirred batch reactor and proposed kinetic models based on activity for the esterification reaction. The experimental results, in agreement with the previous studies, revealed that increase in temperature and catalyst concentration enhanced the reaction rate [197]. However, increase or decrease in the rate of a particular esterification reaction upon changing the temperature is dependent upon enthalpy of the reaction.

Under given conditions the amount of heat absorbed or released by the system is termed as change in enthalpy (ΔH). This parameter determines whether a reaction is exothermic or endothermic depending upon the heat required or released by the system. Enthalpy of reactions for some esters taken from the NIST Chemistry Webbook [198] is given in Table 7 [198]. The magnitude of energy requirements in a reversible reaction can be calculated using various thermodynamic parameters including enthalpy (H), entropy (S) and Gibbs free energy (G) for both reactants and products in a reaction medium. Change in Gibbs free energy (ΔG), enthalpy (ΔH) and entropy (ΔS) define the difference of energy states for transforming reactants into products. For a catalyzed reaction, the interaction between catalyst and substrates is a function of different forces of attraction including van der Walls, covalent, hydrogen, hydrophobic and electrostatic bonds. The type of attraction between molecules can be examined via ΔG, ΔH and ΔS. These thermodynamic functions are function of state as they only rely on the state of system under consideration and do not depend on how the system came into being. Change in Gibbs free energy (ΔG) in a chemical reaction is the amount of energy available to do work as the reaction moves from the initial concentration of reactants and products towards equilibrium. Rise in entropy of surroundings is expressed as ($-\Delta H$/T) and that of system is represented as (ΔH/T) [199]. Change in Gibbs free energy for any spontaneous reaction under constant temperature and pressure is expressed as shown in Eq. (5).

$$\Delta G = \Delta H - T.\Delta S \tag{5}$$

Negative values for change in Gibbs free energy (ΔG), enthalpy (ΔH) and entropy (ΔS) indicate spontaneous and exothermic nature of a catalyzed reaction. Change in entropy (ΔS) for a reaction may either be positive or negative. A negative magnitude shows quick and easy formation of a catalyst-substrate complex leading to significant entropy loss. The formation of activated complex indicates loss of freedom as the transition state formed by reacting species has an ordered state compared to the reactant molecules in ground state. Entropy loss of a system is mainly attributed to the gradual consumption of reactant as the reaction proceeds and also to the release of rotational and translational energies common for a catalyzed reaction. For change in enthalpy (ΔH) of a reaction a positive value indicates that an energy input in the form of heat is required to elevate the energy level of reactants for their transformation to transition state before product formation. Positive value for ΔG indicates that the reaction is endergonic and non-

Table 7
List of esters with corresponding enthalpies of reaction [198].

Compound	$\Delta_r H^o$ (KJ mol^{-1})
Methyl acetate	−9
Ethyl acetate	−6
Methyl benzoate	−5
Ethyl crotonate	+1

spontaneous in nature [199,200]. Esterification is either slightly exothermic or endothermic, depending upon the structure of the reacting carboxylic acid and alcohol.

Increase in the value of rate constant upon increasing temperature of the reaction is reported in various studies within literature. [186,188,192]. However, there are some exceptions in the equilibrium constant's dependency upon temperature in use of carboxylic acids with varying chain length as reported by Bankole. According to the author, in an auto-catalyzed esterification reaction long chain carboxylic acid (linoleic acid) deviates from the trend expressed by short chain carboxylic acids whose equilibrium constant value increase with increase in temperature. The Keq value for the long-chain carboxylic acid increases non-linearly as the temperature increases from 373 K to 473 K. However, as the temperature increases from 523 K to 623 K, the K_{eq} value shows a gradual decline. The reason described by author for this trend is the polyunsaturated nature of linoleic acid and decomposition and thermal degradation process that might have taken place at high temperature [201].

A model based on comprehensive data of reaction kinetics and reactor configuration can serve as an extremely useful source for the optimization of esterification reaction operation [202,203]. Still not all esterification reactions exhibit the same undemanding mathematical treatment. In a study, using 2,3-butanediol and acetic acid with sulfuric acid catalyst for esterification, the reaction advances with two pairs of reversible reactions occurring successively with almost equal speeds not conforming to any simple first, second or third order rate law equation [204]. Empirical rate laws developed from another kinetics study performed using sulfuric acid catalyst in concentration of 0–0.14 wt % with 1-butanol and acetic acid reactants in a ratio of 3:19.6 permitted estimation of the value of the rate constant with a deviation of 15.3% from the molar ratio of reactants. Similar such studies have been carried out on the formation of other esters in the presence of sulfuric acid catalyst at varying temperatures [58].

Effect of molar ratio

Berthelot and Saint-Gilles in 1862 were the first chemists who demonstrated the reaction between an alcohol and carboxylic acid to form an ester and water [205]. In this reaction they found out that when equimolar quantities of both organic acid and alcohol were made to react, the reaction proceeded until only two-thirds of the acid had reacted and then came to a halt. Similarly, when equimolar quantities of ethyl acetate and water were heated together, the hydrolysis of the ester ceased after nearly 1/3 of the ester was consumed by hydrolysis. By varying the molar ratio of alcohol to acid, ester yields more than 66% were achieved due to the equilibrium change. The outcomes of the reaction are in line with the mass action law i.e. K = [ester] [water] = [acid] [alcohol]. However in various cases, the equilibrium constant is affected by different factors like temperature, proportion of the reactants [206] and salt buffering.

The stoichiometric ratio for esterification is 1:1, meaning one mole of an acid requires one mole of alcohol for the reaction to take place [207]. Since the reaction is equilibrium limited, increasing the concentration of one of the reactants disturbs equilibrium and pushes it in the forward direction according to Le Chatelier's principle. Generally, alcohol is required in greater quantities if the reaction is to be forced towards product formation [208]. Using alcohol in excess also helps to decrease the viscosity of the reaction medium in cases where the density difference between reactants is large. This acts to increase the area of contact between the reactant [209]. Alcohol to oil molar ratio is one of the most significant factors in determining the product yield in esterification reactions. Increase in conversion obtained by increasing molar ratio has been reported frequently in literature related to esterification reactions [210–212]. However, there is a limit to using alcohol in large excess. For different experiments, increasing the alcohol concentration beyond certain limits either decreases the conversion or does not show any significant increase. Zheng et al. carried out esterification of oleic acid with ethanol using a surfactant combined with an ionic liquid catalyst. Highest conversion 94.6% was achieved at molar ratio 3:1. Yet, further increase to 3.5:1 caused the conversion to drop to 92% [213]. The excess amount of alcohol dilutes the reaction mixture, causing the concentration of the catalyst to become very low. Furthermore, alcohol molecules deactivate catalysts by binding to their active sites. Thus, the recovery of non-reacted alcohol is difficult, leading to material wastage and increased separation costs [208,214]. The optimum concentration of alcohol varies for each reaction and therefore needs to be determined for the reaction to achieve desired results.

The use of equimolar amounts of acid and alcohol for esterification has been reported in several studies to achieve high conversions. These reactions however, take longer to complete or require special conditions e.g. elevated temperatures and use of special catalysts [66,215,216].

Ester volatility

Generally, esters can be put into three broad categories depending upon their volatility. (1) Highly volatile esters, such as methyl formate, methyl acetate, and ethyl formate, have characteristically low boiling points by comparison to their corresponding alcohols, hence can easily be separated from the reaction mixture by the process of distillation. (2) Esters with medium volatility have the ability to remove water produced by distillation. Examples are ethyl, propyl, butyl, and amyl acetates, propyl, butyl, and amyl formates, and the methyl and ethyl esters of propionic, butyric, and valeric acids. Sometimes azeotropic mixtures containing alcohol, ester, and water are produced. This category can be divided further. In the case of ethyl acetate, all of the ester leaves the system as a vapor mixture with alcohol and part of the water, while the balance of the water stays in the system. With butyl acetate, the balance of the ester persists in the system while all of the water produced evaporates -- removed overhead with some of the ester and alcohol. (3) Low volatility esters are achieved through several types of esterification. In reaction systems where esters are produced from butyl and amyl alcohols, water is eliminated as a binary azeotropic mixture with alcohol. To form esters of lower alcohols, it may be required to add a hydrocarbon such as benzene or toluene to elevate the volume of water distilled. High boiling alcohols, i.e., benzyl, furyl, and β-phenyl–ethyl, need some extra azeotropic liquid in order to withdraw water by distillation [206].

Methods of esterification reaction

To enhance the rate of reaction and conversion of the esterification, several methodologies have been developed and adopted. In the next section, different methods of esterification are critically reviewed.

Microwave assisted esterification

Microwave heating is finding extensive applications in synthetic chemical industry as it has become a widely accepted tool for enhancing the product yields and accelerating the reaction rates while being a safe approach towards heating the chemical mixtures at elevated temperatures [217]. Conventional heating methods for ester production provide uneven heat distribution and slow heat transfer making preheating and reaction time rela-

tively longer. Microwave irradiation for chemical synthesis based on energy transfer via electromagnetic waves requires lower energy input for heating and shorter reaction time as compared to conventional heating. When a reaction medium is irradiated with microwaves, alcohol being a polar molecule aligns with the changes in magnetic field produced by microwaves. Interaction between electric field and molecular dipoles causes molecules and charged ions to rotate rapidly and heat is produced due to molecular friction. High temperature at the local reaction site of catalyst surface is most likely responsible for fast reaction rate. Microwave irradiation directly interacts with the reactant and solvent molecules ensuring efficient heating of the system and fast conversion into the product as shown in Table 8. In microwave treatment, both reaction time and energy input is reduced [218] because real reaction temperature is higher than the average temperature of the medium as a result of localized superheating effect produced by the interaction between molecules and microwave energy [41].

Fig. 4 shows the synthesis of methyl levulinate [219], methyl salicylate [53] and ethyl ferulate [59] giving commendable yields under microwave irradiation in less than half an hour. Heating via microwave irradiation has been reported to facilitate several acid and enzyme based esterification reactions with large scale microwave assisted esterification deemed feasible for batch systems [220,221] or for continuous flow reactor [222,223]. Binal et al. reported 93.63% conversion using sulfuric acid catalyst [224], Marwan et al. demonstrated use of activated zeolite catalyst achieving 95% conversion [225], Saimon et al. studied titanium sulfonated carbonized glucose catalyst reporting 99.63% ester yield [226], Bansode and Rathod showed 5-fold decrease in time required to achieve 95% Isoamyl butyrate yield when microwave technology was used in an enzyme catalysed esterification [227]. Solid catalysts such as ion exchange resins [11,228,229] zeolites [230] and carbon based acid catalysts work effectively for ester production under microwave irradiation requiring much less time for attaining desired yield compared to conventional methods. Ning and Niu performed an experiment for the production of biodiesel via esterification in the presence of bamboo based acid catalyst. 97.31% yield under microwave irradiation method was achieved compared with 63.94% obtained using traditional method after 1 h [231]. In another study carried out by Quitain et al., for FAME production, comparison studies revealed ~80% conversion by microwave method compared with ~ 20% obtained via conventional technique after 5 min of reaction using graphene oxide catalyst [232]. Studies based on autocatalysis under microwave irradiation have also been performed for esterification reaction. This technique has been regarded as green, ecofriendly, safe and reliable as it prevents catalyst contamination observed in other chemical processes [233]. High product yield achieved under these conditions were however attributed to elevated reaction temperatures. Keramat and Golmakani observed high reaction rates and pronounced sesamyl butyrate yield when microwave heating temperature was increased from 313 K to 343 K raising product yield from 82% to 98% respectively [234]. In a similar study performed under no catalyst condition, phytosterol yield increased from 58.7% to 89.6% when temperature was raised from 393 K to 443 K at reaction time of 50 min. Also, raising microwave power affected the conversion significantly in this experiment [235].

Microwave technology harbors several advantages in terms of product synthesis as evidenced from various experimental studies performed at laboratory scale. However, one challenge is high investment required for its installation in plants that still heavily rely on conventional methods. Its incorporation into the existing engineering would entail high replacement costs. Scalability of microwave treatment is a problem due to various factors such as restricted penetration depth of radiation into the reaction medium, heat loss, additional reflection of microwaves and changes in absorption. The use of microwave reactors is avoided for volumes greater than a few liters because of these complications [236]. Penetration depth of the microwaves into the absorbing materials is only a few centimeters at 2.45 GHz. This limitation causes the reagent or solvent in the center of a large vessel to heat by convection and not by in core direct microwave dielectric heating preventing scale up of reactions with microwave intensification [237]. Another issue related to this technique is difficulty in the assessment of reproducibility of reactions carried out in domestic microwave devices without appropriate pressure and temperature controls prior to the introduction of microwave reactors appropriate for laboratory use (until 2000). Incomplete description of reaction conditions, insufficiently reported microwave device settings and the use of different microwave devices raises reproducibility issues with regards to earlier research on microwave assisted organic transformations and limit the application of such reactions [238].

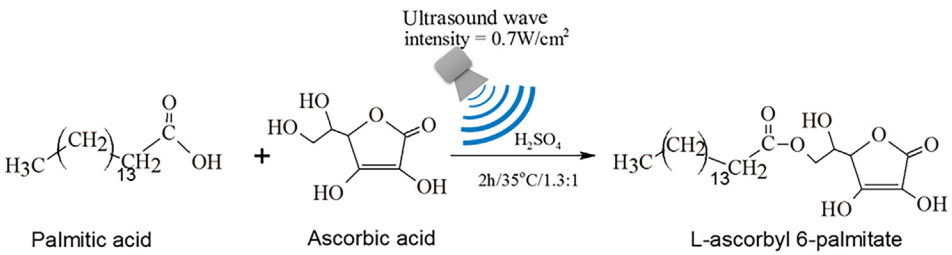
Contrary to the generally held opinion regarding low power consumption of microwave methods, the energy efficiency aspect of microwave assisted organic synthesis is questionable as its assessment is a complex task that requires taking different factors into account such as heat absorbance characteristics of reaction mixture, time taken for a reaction to reach completion, the particular type of microwave instrument used (single or multimode), the volume of reaction mixture heated, etc. Thus, based on some studies carried out regarding energy efficiency of microwave technology, it cannot be established with certainty that microwave treatment is more efficient in terms of energy consumption as compared to conventional methods. Capital intensiveness, without

Table 8
Microwave assisted esterification performed in the presence of acid catalysts under optimum conditions.

Reactants	Molar ratio Alcohol/ Acid	Catalyst	Temperature (°C)	Reaction time (min)	Conversion (%)	Ref
Methanol Benzoic acid	1.5–2:1	Methanesulfonic acid (CH_3SO_3H) supported on alumina (Al_2O_3)	80	8	98	[241]
Methanol Oleic acid	9:1	[Bmim]HSO4	120	30	94	[242]
n-butanol Maleic acid	3:1	Amberlyst-15	70	60	62.6	[243]
Ethanol Oleic acid	2:1	–	200	360	97.62	[42]
i-propanol 3-fluro benzoic acid	3:1	Sulfated alumina-zirconia (SAZ)	100	15	94	[244]
1-propanol Benzoic acid	1:1	Triphenylphosphine and iodine	85	30	93	[245]
Methanol Oleic acid	20:1	Sulfated zirconia	60	20	>90	[246]
Ethanol Ferulic acid	6:1	H_2SO_4	75	3	95	[59]
1-hydroxy-3,4-dimethyl-3-phospholene 1-oxide Dodecanol	12:1	–	230	120	95	[247]
Methanol Oleic acid	5:1	Sulfonated hydrothermal carbon	100	60	97	[248]

certainty of low power consumption, militates against the implementation of this technology for large scale production [239,240].

Sonication assisted esterification



(6)

Ultrasonic technology has emerged as an attractive option for providing energy for organic reaction as it offers safety and ease of performance [249]. This technology engenders the cavitation effect that enables improvement in mass-transfer rate and mixing between the phases. Reactions carried out via this method have been reported to give higher product yields in shorter time, faster reaction rates and better selectivity [250,251]. Movement created by the sound source is transmitted to the particles of the medium that oscillate in the direction of waves producing both longitudinal and transverse waves. This causes the molecules of the reaction medium to vibrate, increasing and decreasing the distance between molecules during alternate cycles of rarefaction and compression. Average distance between molecules decreases during compression and increases in the rarefaction cycle. When the distance between molecules exceeds the critical molecular distance required to keep the liquid intact, the fluid breaks down, forming cavities – bubbles that comprise vapor of the liquid. Gradual growth in the bubble size that ultimately leads to its collapse results in high temperature (~4700 °C) and pressure changes (~10 Pa) along with sending shock waves that influence reactivity. The solvent vapors suffers fragmentation releasing reactive species concentrated at the interface, leading to intermolecular reactions as shown in Fig. 5 [252,253].

Ultrasonication aids in speeding up esterification process by increasing the miscibility between oil and alcohol that ultimately reduces reliance on large quantities of catalyst. In case of heterogeneous catalyst ultrasound energy increases the reactivity by breaking down the solid catalyst into fine particles that increases the surface area and in turn availability of active site thus improving catalyst performance. It also sufficiently enhances the interaction of catalyst with reaction components by narrowing the boundary zone between them thus assisting in overcoming mass transfer issues and increasing the reactivity several fold higher [254]. Vartolomei et al. presented a comparative study for the production of isoamyl acetate using both conventional and ultrasound method using acidic ion-exchange resin. 30% increase in ester production was observed using sonication method after running both experiments for 2 hours [255].

Ultrasonic assisted esterification of palmitic acid with vitamin C in the presence of concentrated sulfuric acid as solvent and catalyst produced enhanced ascorbyl palmitate yield as shown in Eq. (6) [256]. Direct oxidative esterification of aldehydes and alcohols using graphite oxide and oxone (derived from potassium peroxymonosulfate) reported mild reaction conditions, short reaction times, cost-effectiveness and simple product isolation [257]. Enzyme catalyzed esterification in the presence of ultrasound irradiation has demonstrated similar results [258–260].

Process intensification tools like ultrasonication technique offer benefits in terms of green synthesis by offering better process timing. Time required for downstream separation and process treatment cycles is reduced and wastewater generation is significantly minimized [254]. Khan et al. reported 70% decrease in production time by performing ultrasound assisted esterification for enzyme catalyzed production of n-butyl palmitate [261].

Despite offering ease of operation and enhanced mass transfer rate as proven by different laboratory scale experiments, ultrasonication carries big challenge in terms of its applicability and installation in large scale industrial processes. Ultrasound application requires greater input of energy for its operation raising the overall cost of production [262]. Additionally, use of custom made equipment for specific applications is cost intensive. Direct contact between certain liquid media and ultrasound horns is reported to cause problems in some applications. Absence of large ultrasonic reactors is an obstacle in utilization of this technology at commercial levels [263].

Membrane technology

Improvement in reaction efficiency by using a reactor equipped with a membrane permeable to products leads to a favorable shift of the chemical equilibrium. Esterification performed in batch reactors yields low conversions because of thermodynamic equilibrium thereby generating esters in small quantities. Improvement in the yield of desired product requires driving the equilibrium towards ester production either by addition of excess amount of alcohol in the system or use of separation processes such as reactive distillation for the continuous removal of one of the products of the reaction. Addition of excess amount of reactant is an inefficient approach as it leads to the requirement of large reactor volume and creates additional cost of recovery of unreacted alcohol along with separation of product from diluted stream. Reactive distillation, though a conventional process commonly employed in plant operations, carries certain inconveniences such as the requirement of large difference between the volatility of reactants and the products (usually not the case in most of the reactions). Additionally, formation of azeotropes is reported in many reaction processes. Reaction and distillation temperatures oftentimes do not match. This can cause complications in process performance with high consumption of energy. Its use is also dis-

couraged when dealing with temperature sensitive chemicals or biocatalysts [28,264].

Pervaporation membrane reactors (PVMR) are emerging as a competitive alternative to distillation. They function under mild operational conditions, suitable for heat sensitive reaction products and close boiling azeotropic mixtures. They also minimize product purification requirements [265,266]. Unlike reactive distillation that is based on variation in volatilities of substances, pervaporation depends on the solubility and transport rate of each component. Pervaporation membrane reactors allow very selective removal of water from reaction medium with two possible configurations: reaction and separation performed in two stages in different reactors termed as ex-situ pervaporation or both steps carried out within a single integrated unit termed as in-situ pervaporation. In the former method, reaction takes place in a batch reactor followed by an external unit built in the recycle with membrane for removing water (Fig. 6) while within a single unit reactor reaction and separation occur simultaneously [267]. A single unit reactor may employ an inert membrane with suspended catalyst in reaction mixture as in case of pervaporation membrane reactor (PVMR) or employ a functionalized catalytic membrane for performing dual functions of catalysis and separation in pervaporation catalytic membrane reactor (PVCMR) [268] as shown in Fig. 7. Several studies favor the use of a pervaporation membrane reactor (PVMR) over conventional batch reactor owing to its benefits of catalyst recovery from reaction medium and superior conversion rates attributed to simultaneous reaction and water removal from the system. A comparative study performed by Nigiz for the production of methyl laurate ester PVMR showed 22.5% conversion improvements compared to a batch reactor. PVMR even performed better than PVCMR due to the loss of active sites in catalyst coated polymer membrane [268]. Another study reported enhancement of 19% in conversion compared to traditional equilibrium reaction when a novel ionic liquid functionalized catalytic composition membrane IL-CCM was used with enhanced catalytic stability [269]. Wang et al. reported high product yield of 98.4% in 12 h upon employing pervaporation membrane with porous catalytic layer in a pervaporation catalytic membrane reactor (PVCMR) that greatly enhanced esterification with reduced mass transfer resistances [253]. Sun et al. achieved 96% ester yield after 16 h using

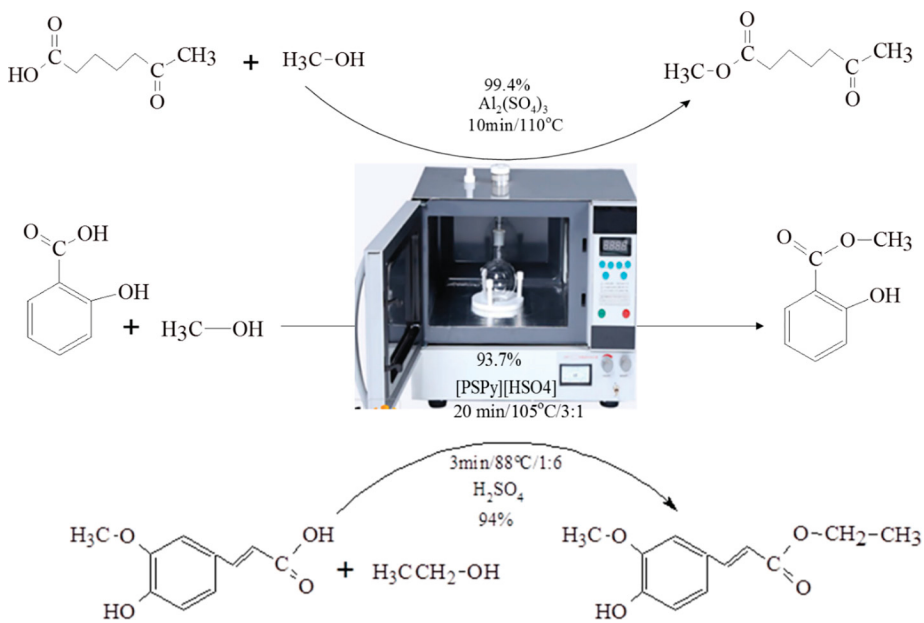


Fig. 4. Microwave irradiation for the production of methyl levulinate, methyl salicylate and ethyl ferulate.

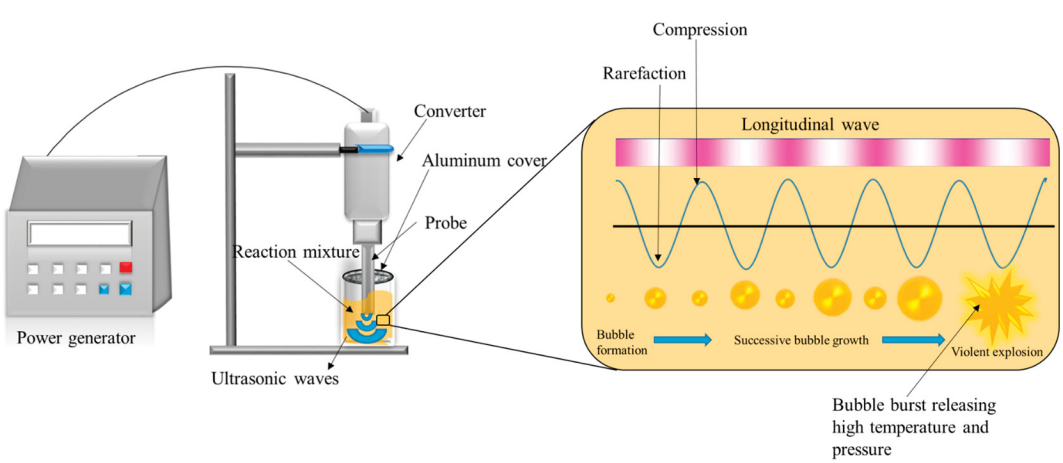


Fig. 5. Bubble collapse enhancing mass transfer between oil and alcohol by sonication method.

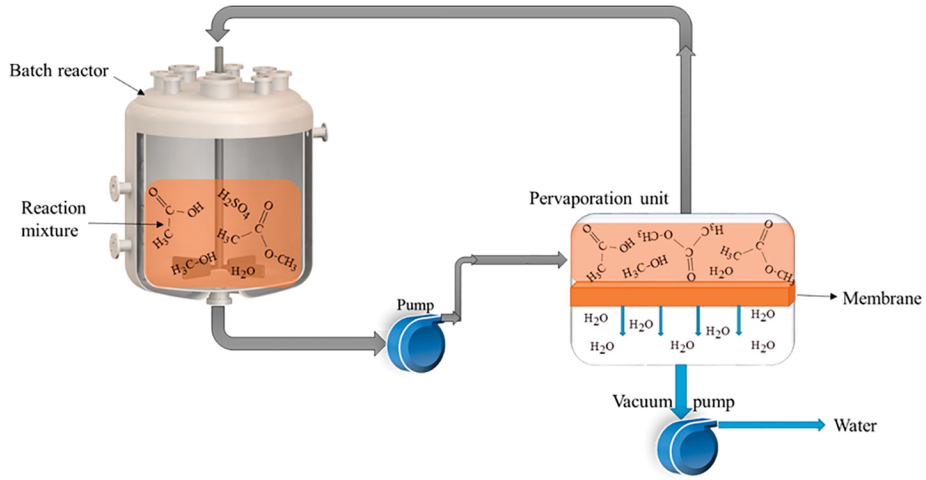


Fig. 6. Batch reactor combined pervaporation for water removal from reaction mixture.

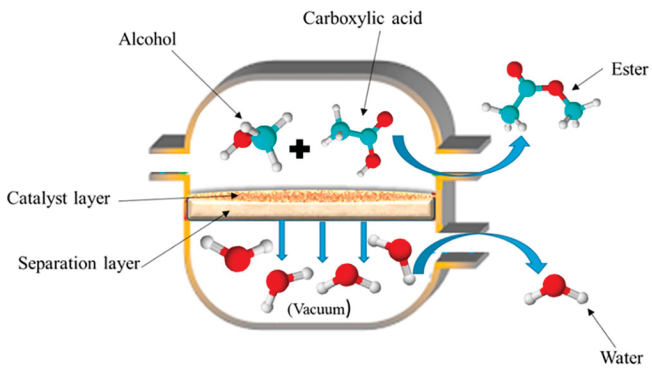


Fig. 7. Pervaporation in a single unit using catalytic membrane.

dual functional composite membrane (DCM) reporting excellent membrane stability after 5 runs [270].

Multiple studies have shown the application of pervaporation by using polymeric, ceramic, zeolite and other inorganic hydrophilic membranes for enhancing the ester yield [271–274]. Polymeric membranes used for pervaporation are limited by solvent and temperature stability affecting their performance in the long run. Hydrophilic polymeric membranes show swelling behavior at high water concentration owing to their good dehydrating ability and a strong affinity towards water molecules. Swelling alters membrane properties resulting in lower selectivity and higher permeability [275]. Ceramic membranes, in contrast, offer excellent structural integrity and stability but are prone to poor selectivity and limited selection of pore sizes [276]. Other significant drawbacks of pervaporation are slow rate of mass transfer, low retentate temperature, high pressure drops, temperature and concentration polarization [277].

Microbubble technology as an alternate technique for esterification

Microbubble mediated mass transfer has been studied for esterification reactions in several applications such as ethyl acetate production [278], biodiesel production using oleic acid [19] and a with bubble phase ozone catalysis [32]. The rising cloud of microbubbles creates a stirring effect, further, increasing the contact area among reagents [279]. Alcohol is vaporized at its boiling point. The vapours produced are fed, in the form of microbubbles, to a bubble reactor using a diffuser as shown in Fig. 8. The bubble reactor contains the other reactant, carboxylic acid etc., as the alcohol vapour bubble rises through liquid, its size reduces due to dissolution of vapour in the liquid. In order to understand how microbubbles aid in increasing contact area between reactants the "localized bubble interface" needs to be understood. The liquid drag force due to high momentum transfer gives rise to greater retention time of microbubbles inside the liquid phase. Hence, alcohol in the vapor phase, naturally in high excess, reacts at the bubble interface with acid, which is naturally in high excess. The presumption is that the organic acid is barely volatile, so contacting only occurs at the bubble interface. Since bubbles are continuously injected and also continuously removed by bursting at the top of the liquid layer, this highly non-equilibrium contacting pattern is maintained. Since, alcohol vapor is fed in the form of microbubbles, it is not present in excess in bulk to establish the equilibrium. Commonly, insolubility of alcohols and organic acids maintain phase separation so that contacting is only at the microbubble interface. Thus, at the skin of the bubble- vapour liquid interface- alcohol is always present in excess pushing the reaction in forward direction as shown in Fig. 14 [280].

The temperature of the bubble reactor is maintained at the boiling point of the alcohol (around 70 °C). The unreacted alcohol leaves the reactor as the bubble bursts at the surface, preventing the accumulation of alcohol. While the alcohol is transferred from inside of the bubble, the volatile products tends towards the center of the bubble. When the microbubbles bursts, for instance, the pro-

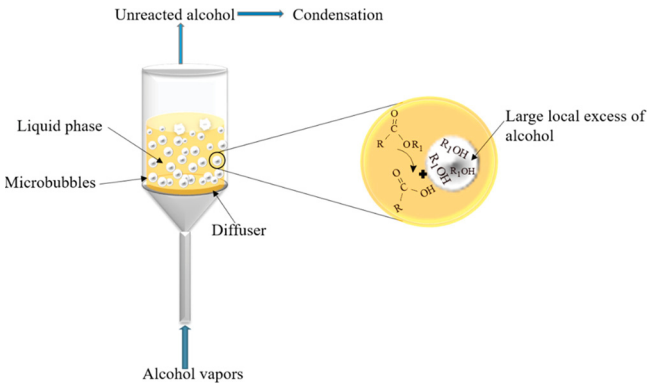


Fig. 8. Illustration of microbubble mediated enhanced mass transfer between alcohol and carboxylic acid.

duced water leaves the system as well. Generally, the injected microbubbles are anhydrous, so water vapour is typically present below saturated humidity. However, there are two possibilities for the main the product-ester. If the product of esterification reaction is a high boiling point reagent such as biodiesel, it would not leave the reactor along with alcohol and water. However, low boiling point esters such as methyl acetate or ethyl acetate would leave the reactor. In either case, the product and/or by product leave the system, pulling the equilibrium in the forward direction as well. The unreacted alcohol can be condensed and recycled [19]. A conversion of 79.95% of ethyl acetate in 35 min has been reported as compared with 65% obtained using typical reactive distillation column [280]. Similar study reports 97% conversion achieved in 30 min upon reacting oleic acid with methanol using microbubble reactor that released methanol bubbles within the size range of 200–600 um. Higher yields can be obtained by enhancing mass transfer rates without large energy expenditure in contrast to the conventional methods where only 80% conversion is achieved in 312 min [19]. Significantly higher conversion and rate of reaction can be explained on the basis of higher residence time and high pressure and temperature available at the bubble surface as well.

As compared with the conventional method, the reaction is carried out in a semi-batch fashion in microbubble technology. The rising velocity of microbubbles plays a vital role. Larger bubbles, with a diameter of 1–3 mm, tend to rise quickly. The gas enclosed in the bubble escapes at the surface of the liquid without coming in contact with it. Microbubble size ranges within diameters less than the several tens of millimeters common to macrobubbles [281]. Bubbles with sizes of several 100 μm or less have spherical shape and rise as rigid spheres. It is worth noting that microbubbles with ellipsoid shape rise rapidly. However, owing to their smaller size tend to remain for longer periods of time in liquid. If comprising soluble gas, as they rise, their size decreases gradually within subsaturated liquid and disappear eventually due to the dissolution of enclosed gas in the surrounding liquid [282]. Macrobubbles tend to coalesce, making even larger bubbles. This, further reduces mass transfer. Coalescence of microbubbles become more predominant at higher flow rates as the flow regime is shifted from laminar to heterogeneous bubbly flow regime [283]. However, microbubbles injected with little kinetic energy rise in a laminar flow regime, which ensure low coalescence and increased mass transfer as shown in Fig. 9.

One of the reasons for achieving high conversion and rate of reaction using microbubble mediated mass transfer is high surface energy and high temperature and pressure available at the bubble (vapour)/liquid interface. Higher internal pressure is a typical characteristic of microbubbles [282]. The vapour pressure inside a microbubble exceeds the liquid because of its smaller diameter with surface tension effects dominating, as governed by Young Laplace equation:

$$P = P_1 + 4\sigma/d \tag{7}$$

where P is pressure of the gas, P_1 is the liquid pressure, σ is the surface tension of the liquid and d is bubble diameter. For example, a 1 μm microbubble possesses internal gas pressure of 390 kPa, which is almost three-fold excess above atmospheric pressure. As described earlier, a rising microbubble comprising soluble gas decreases in size and disappears eventually inside a sub-saturated liquid. As the bubble gradually shrinks, the internal pressure continues to increase and a high pressure spot is potentially produced in the final stage of collapse, similar to cavitation bubbles. In the last stage of collapse, if the collapsing speed is high enough, the process can be assumed to be an adiabatic compression process. During this process, the temperature inside the bubble rises sharply as there is little heat transfer between the microbubble and its surroundings, due to laminar boundary layers. Henry's law suggests that a bubble with rising interior pressure experiences greater amounts of dissolved gas surrounding, thus causing the gas within the microbubble to dissolve during shrinkage. Higher inner pressure, high temperature also increases gas/vapor solubility and hence increases mass transfer. All these parameters make microbubble technology a competitive methodology for esterification reaction. However, the benefits of microbubble mediated mass transfer could only be exploited if microbubble could be produced cost effectively. There are several methods available which needs to be reviewed critically.

Microbubble generation methods

Microbubble generation is carried out via different methods based on decompression, gas–water dispersion employing a medium, gas–water circulation [284] and other means such as ultrasonication and electrolysis [285]. Diameter and size distribution of bubbles produced by different methods is significant is different. [286]. Two commonly used methods of bubble production are described in the following sections.

Decompression

Most of the technologies for microbubble production are based on decompression method. In this method water supersaturated with air under high pressure is forced through very tiny valves. As the pressurized gas is highly unstable it will quickly escape through water upon sudden decrease in pressure resulting in instant release of many microbubbles. System employed to carry out this process usually contains a tank and pump as in Dissolved Air Flotation (DAF) [282]. DAF is commonly used for biological wastewater treatment where 30% of the purified water is recycled through a pressurized vessel and then saturated with 70–80% air at high pressure of 5–6 bar or 0.4–0.5 MPa. This pre-saturated water is then decompressed through injection nozzles or expansion valves in a flotation cell. The microbubbles released as a result readily attach themselves to the solid particles and rise to the surface of the liquid [287,288] as shown in Fig. 10. These bubbles

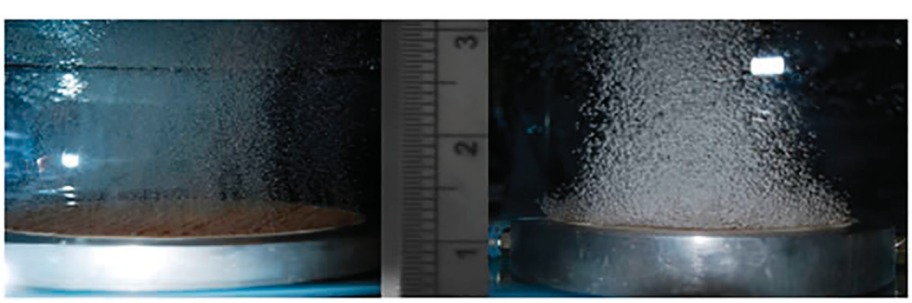


Fig. 9. Microbubbles generated without fluidic oscillator (left) and with fluidic oscillator (right) under laminar flow.

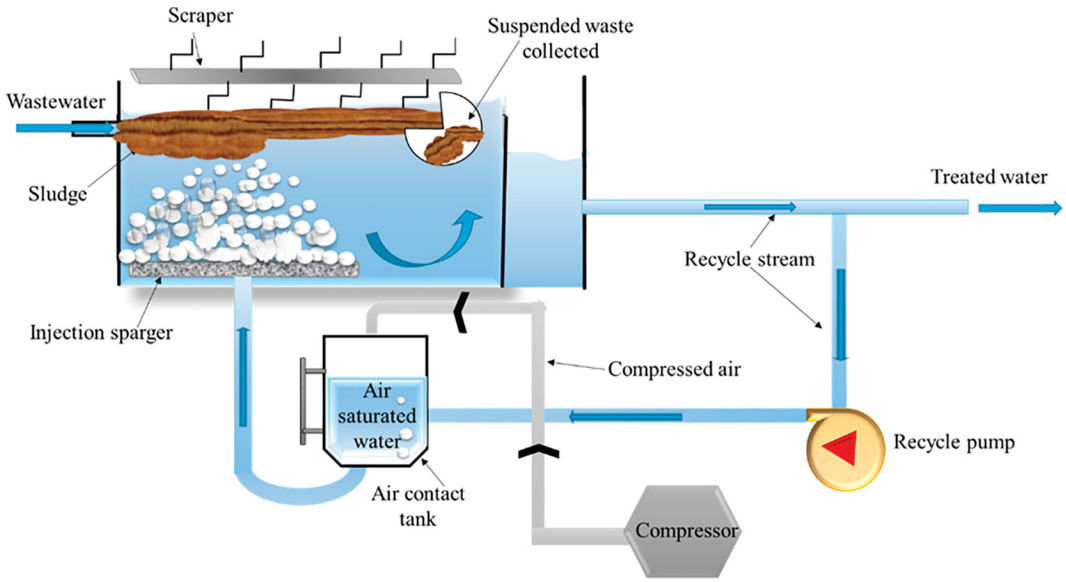


Fig. 10. Dissolved air flotation (DAF) process.

range in diameter from 10 to 120 μm with a mean value of 40 μm. Removal of low density particles that have tendency to settle very slowly or float, like clay size materials and algae, from potable water is carried through DAF often serving as an alternative to sedimentation[286]. Additionally, DAF has applications in mining and mineral processing industries [289].

Gas-water dispersion

Another technique that is used for generating microbubbles is gas- liquid dispersion using a medium. Dispersed air flotation or Induced air flotation (IAF) is a technique that makes use of bubble diffuser that unlike dissolved air flotation, where bubbles are produced at the bottom of the column, requires compressed air forced through pores of fixed size to produce bubbles [286]. IAF carried out via sparger air injection or mechanical agitation is occasionally used for treatment of wastewater with colloidal matter as it yields bubbles that are larger in size than those produced by DAF [287]. Different studies for modification in the process of dispersed air flotation have been carried out for the release of microbubbles by the system, such as the introduction of radially discharging funnel shaped nozzle in flotation cell and rotating-flow microbubble generator [287,288].

There are a few studies that deal with the production of microbubbles using gas water dispersion method through membranes. These studies however are limited to aqueous medium and provide the benefit of using commercially available devices and reduced costs of power consumption when compared with technologies like DAF [285]. Shirasu porous glass (SPG) membrane is a type of glass membrane with numerous pores of cylindrical shape that are uniform in size and together form interconnected three-dimensional network advantageous for gas–water dispersion process. Microbubbles are produced using this process by inserting gas under high pressure through the SPG membrane into the liquid phase [284]. Fig. 11 shows bubble formation from pores of a membrane. Several papers have been published regarding study of various factors affecting microbubble formation using SPG membrane by Kukizaki et al. [290–293]. These studies suggest that uniform sized very small bubbles can be obtained using SPG membrane as compared with porous ceramic membranes that produce large size poly dispersed bubbles. Shirasu porous glass membrane serves key benefit of optimizing the size of microbubbles according to required conditions as membrane size and area determines the size and void fraction of microbubbles [284].

Fluidic oscillation

Fluidic oscillation is another low power microfluidic microbubble generation technique that involves air stream provided under low offset pressure that breaks off forming bubble while it is still in the smallest emerging state (hemispherical cap) from the pore of the nozzle via mechanical vibration or air pulse oscillation [279]. This technology works based on fluid oscillations that provide gas flow vibrations generated via an amplifier and a feedback loop. The amplifier contains a special cavity while the feedback loop forms a connection between amplifier's control terminals as shown in Fig. 12. Fluid after passing through the nozzle enters the cavity in the form of a jet that causes the fluid to sweep along in its flow from either side of the jet. Coanda effect causes the jet to lean towards one side of the cavity due to the emergence of low pressure areas around the walls. As a result, a pressure difference is established across the control terminals. This pressure difference changes the path of the jet pushing it into the other outlet by means of a pressure wave produced inside the feedback loop as shown in Fig. 12 [283].

High oscillation frequency is required to generate small bubbles. Oscillation frequency is dependent upon two factors, length of the feedback loop and inlet flow rate [279]. Longer the length of the feedback loop lower will be the frequency, displaying an inverse relationship between the two quantities. However, increasing the inlet flow rate increases the oscillator's vibration frequency that leads to high density microbubble generation. The mentioned conditions that work best for fluidic oscillators are counterproductive in case of steady state flow conditions as increasing the flow rate decreases the bubble density and also leads to bubble coalescence [283]. Other than inlet flow and feedback loop size, the diffuser membrane characteristics also affect bubble formation and separation from diffuser surface. For the early forceful detachment, while the bubbles are still in their pre-mature stage, the use of hydrophobic membrane surfaces must be avoided as they facilitate bubble anchoring to the surface and prolong separation. Also, membrane diffusers with uniform pore sizes in sub millimeter range allows the formation of mono dispersed microbubbles with enhanced mass transfer efficiencies and prolong stagnation time

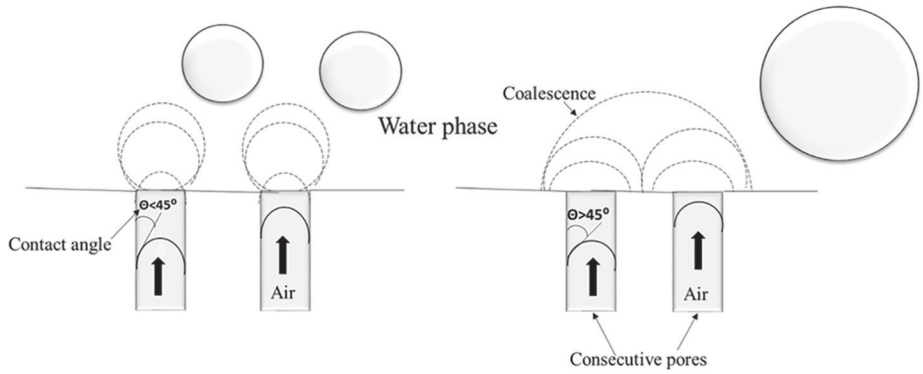


Fig. 11. Microbubble and macrobubble formation from pores of a membrane.

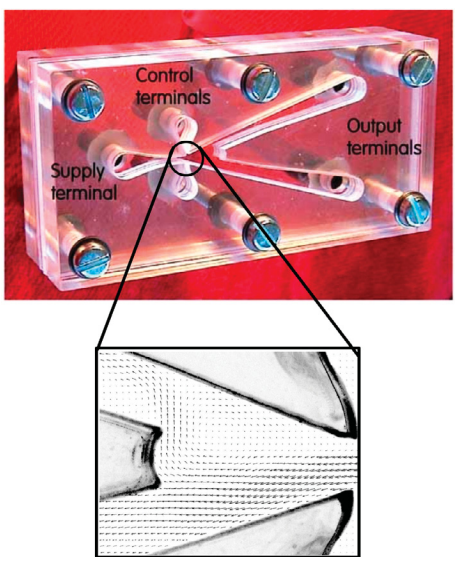


Fig. 12. Construction of a fluidic oscillator with PIV image showing fluid flow diversion into one of the two outlets [279,283].

within the liquid. Once the membrane frequency synchronizes with the fluidic oscillation frequency bubble escapes into the liquid medium [279]. Fig. 13 shows the complete setup for microbubble production in a feed tank by fluidic oscillation.

Fluidic oscillation provides a low cost, reliable option for microbubble formation without requiring over maintenance or modifications in existing aeration systems or relevant gas–liquid process systems. Rehman et al., carried out an experimental study to compare the microbubble generation ability of fluid oscillation technique with steady state aeration system for wastewater treatment. The results obtained for bubble size distribution and mass transfer efficiency revealed that bubbles obtained from fluidic oscillation were in micrometer to millimeter range compared to the bubbles generated in millimeter sizes under steady state flow conditions. Smaller bubble size offered enhanced mixing of the gas within the liquid while requiring low energy input. The technology offered ease of installment within existing aeration systems without requiring extensive modifications [283]. Fluidic oscillation has also been adopted as a patent technology for large scale installment or application to carry out enhanced gas transfer and mixing operations in bioreactors/digesters and for particulate separation systems especially algal floc removal from water [294].

Different microbubble production techniques mentioned above come with certain merits and demerits. The feasibility and application of a technology at large scale demands greater efficiency with reduced costs of assembling, bubble production and power consumption. In DAF, the size of the bubbles generated is very small. While such bubbles are very effective in collecting flocs and small particles and have longer stagnation time, they also have correspondingly small terminal velocities such that the residence time required for all the bubbles to rise to the surface and pass from the flotation cell is relatively long, demanding significantly large vessels [295]. The technique operates with large water recycle that requires significant increase in the volume of flotation cell. Also the necessary requirement of a pressurized vessel along with an air

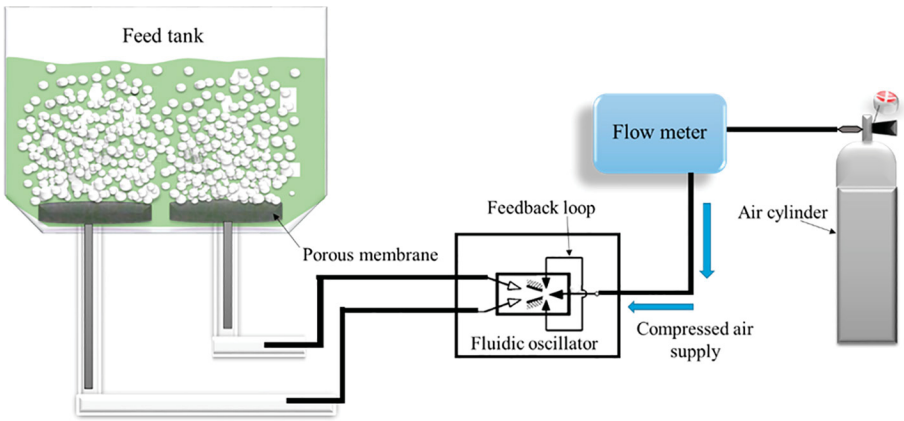


Fig. 13. Microbubble generation via fluidic oscillation.

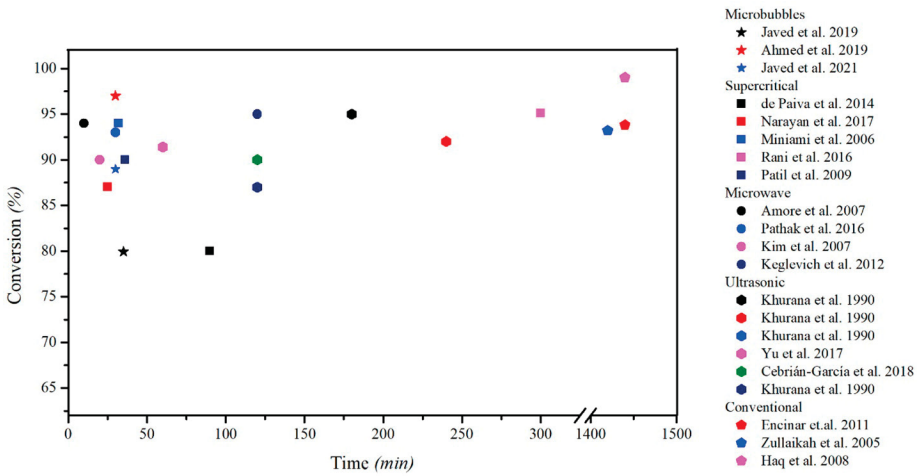


Fig. 14. Comparison of different esterification technique with or without acid-homogenous catalyst.

compressor whose efficiency amounts to only 60% makes it cost intensive [288].

Bubbles produced by conventional IAF technology are relatively larger thus, the flotation system required is much more compact however, bubble size influences the efficiency of bubble-particle collision with larger bubbles leading to poor collision efficiency. Also, mechanical flotation cells in conventional technologies can cause fragile particle breakage due to high shear force [287]. Some advances in IAF technology have managed to produce microbubbles without the requirement of a pressurized vessel and gas compressor with only 10% recycling of treated water thus preventing use of large flotation cells and enabling operation on low power densities [287,288].

Microbubble generation through membrane requires less power, provide narrow bubble size distribution along with the utilization of materials that are available commercially reducing the construction cost [285]. Production of monodispersed micro and nano bubbles is achieved through SPG membrane with narrow pore size distribution offering advantage of controlling bubble size [296]. This technology helps counter the issue of excessive power consumption commonly encountered in ultrasonication and electroflotation techniques [279,285]. However, research is still underway regarding optimization of this technology for large scale application as there are different factors that influence the emergence of bubble through porous membranes [285].

Comparison with conventional and state-of-the-art processes

Comparison of various techniques for esterification reaction with and without homogenous acid catalyst is shown in Fig. 14 [19,37,45,82,245–247,258,280,297,298,300–306]. The graph indicates that conventional process requires longer reaction time to reach higher conversions ~>90% as compared to other methods. Haq et al. demonstrated high conversion of 99% but in extremely long time of 1440 min due to inherent mass transfer problems [297]. Miniami et al. were able to achieve conversion of 94% in 30 min but at the expense of high capital and operational cost of supercritical method [45]. Amore et al. also demonstrated conversion of 94% in just 10 min via microwave irradiation [298]. But this process is highly energy intensive and it's upscaling is difficult. Khurana et al. were able to achieve 92% conversion in 240 min by ultrasonic process but this technique has limited reaction rate with long time to reach high conversion [303].

The conversion of ethyl acetate as reported by Javed et al. apparently seems low −79% in 35 min [280]. However, as compared with conventional method for ethyl acetate gives 65% in 350 min, the microbubble achieved higher conversion in 35 min with 65% in first 10 min. To enhance the overall proves efficiency, this reaction could be stopped at first 10 min for downstream separation. The conversion is low however, the production rate can be increased making the overall process cost effective. In another study Ahmad et al. reported 98% conversion of oleic acid in 30 min by using microbubble [19]. The reported result have higher conversion in shorter period as compared with conventional process such as Zang et al. reported 66% conversion of oleic acid in 420 min by using conventional process [299].

Esterification studies performed thus far using microbubble technology show promising results compared to other techniques. Higher conversions with less energy input are achieved in less than 30 min owing to the high surface area and surface energy of the microbubbles. Reaction occurs in gas/liquid interface which reduces the chance of film formation, a problem usually encountered in conventional methods due to the immiscible nature of reactants. The rate of reaction increases as dynamics of reaction change from diffusion control to kinetic control. Increased mass transfer reduces the reaction time and makes this process suitable for large scale applications.

The process of esterification is a key to multiple product synthesis at industrial level. It constitutes the very basis of chemical phenomena that generates numerous products employed at household and commercial level. Considering the significance of this process its efficiency needs to be boosted in order to achieve high product yield within short period of time while considering environment friendly options to make the process sustainable over time. Esterification being an equilibrium limited reaction has been tested under various conditions in numerous studies published in the past several decades. Catalyzed esterification is generally preferred over non-catalyzed esterification to obtain the desired yield within short period of time without making the process energy intensive due to high temperature requirements in the absence of catalyst. Catalysts broadly categorized as homogeneous and heterogeneous are both studied extensively for their feasibility as both have their pros and cons. Homogeneous acid catalysts commonly utilized in bulk methods are cheap and offer fast reactivity while causing environmental toxicity and posing handling problems. Heterogeneous catalysts on the other hand have benefits in terms of recyclability but are expensive. Experimental studies designed for laboratory scale production report commendable yields obtained from different conventional and non-conventional methods including microwave technology, sonication and novel separation techniques to obtain high yields of purified products. These techniques defying mass transfer resistances accelerating the rate of

reaction though efficient are more or less similar in terms of their non-feasibility when it comes to scaling up for mass production. Cost intensiveness in terms of installation and energy investment are the two major drawbacks that need to be addressed through a technology that can easily be expanded from bench-scale to full-scale industrial production.

Microbubble technology vastly employed in various environmental and separation processes offers a potential option to improve esterification by overcoming mass transfer diffusion limitations while simultaneously cutting down the cost for downstream separation processes. Unreacted alcohol that continuously leaves the reaction mixture prevents the establishment of equilibrium, reduces cost of product separation and purification and can easily be condensed for reuse or recycling within the same system. This technology operates at minimum optimum temperature of 70–80 °C and pressure maintained constant at 25 mbar (0.0025 MPa) without the need for mechanical agitation as is required in conventional methods. High product yields have been obtained in different experimental studies performed thus far with over 90 percent conversion obtained in less than an hour saving overall operation time. Microbubble technology for esterification being economical holds a potential solution to majority of the problems associated with various production techniques mentioned above. This technique has the capacity to be further optimized by incorporating low cost recyclable heterogeneous catalysts along with membranes having greater stability and uniform pore sizes for the production of nano bubbles to enhance the efficiency of the overall process.

Conclusion

Esters, most abundantly prepared by the reaction between alcohols and carboxylic acids, face production limitation due to the formation of byproduct water. This review on esterification offers an insight into the various advancements carried out to promote efficiency and to overcome challenges related to product hydrolysis, by using water removal techniques and numerous catalysts have been reported for their effectiveness in providing enhanced yields along with the emerging green technologies that rival the conventional methods by avoiding environmental degradation in methods of production, sometimes breaking free from the requirement of a catalyst to make the reaction proceed faster. Technologies that provide higher yields in shorter periods of time with cost effectiveness are well sought after. Recent introduction of microbubble technology to this field has offered a cost effective means to overcome the resistances of mass transfer by enhancing the area of contact between the reacting substances. Mild reaction conditions involving relatively lower temperature, shorter reaction time, fast conversions, and absence of mechanical agitation along with the elimination of additional cost of downstream separation make this method a valuable addition to the advanced technologies for ester production.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

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