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LACTIDE AND LACTIC ACID OLIGOMER SOLUBILITY IN CERTAIN SOLVENTS

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Abstract

Crude-L-lactide solubility in ethanol, butanol, isopropanol, carbon tetrachloride, o-dichlorobenzene, bromobenzene, chlorobenzene, brometane at 23°C, L-lactide solubility in ethylacetate, butyl acetate, vinyl butyl ether, chlorobenzene, chloroform at 0, 23, 40°C, solubility of L-lactic acid oligomers with different molecular weight in ethyl acetate, butyl acetate, chloroform, benzene, cumene, toluene, carbon tetrachloride, ethanol, acetone, butanol at various temperatures have been investigated. Literature data of lactic acid solubility in different solvents are presented.

Keywords: lactic acid; lactide; oligolactic acid; biodegradable polymers; solubility.

1. Introduction

Nowadays the most large-tonnage biodegradable polymer is polylactic acid (polylactide) as this polymer is widely used as a raw material for environmentally-friendly packaging material production in many countries [1-2]. Such packaging is able to save consumer properties throughout the operating period and be sufficiently fast composted under various environmental factors (sunlight, oxygen, moisture and soil microorganisms, seawater) to substances which are harmless to the environment (carbon dioxide, water, humus). Requirements for the results of biodegradable polymer composting are regulated by European Standard [3].

Polylactic acid and its copolymers are also widely used for producing various medical products (sutures in surgery, implants, pins, bandage, screws in orthopedics, matrices for tissue engineering, materials for dental and long-acting dosage forms in pharmaceutical industry) as they are biocompatible with a human body and are gradually resorbed in it into harmless substances [4-5].

It is important that lactic acid (LA) is produced by enzymatic fermentation of renewable natural resources such as glucose, sucrose, sorghum juice, molasses, a mixture of raw sugar, refinery molasses, beet molasses, hydrol, lactose, starch hydrolysis, cellulose-containing materials and waste from food industries [6-7]. LA is the initial material for polylactic acid synthesis.

When LA aqueous solution is used as a raw material, synthesis generally includes the following steps: concentration of the LA solution; oligomeric LA (OLA) synthesis; crude-lactide synthesis; lactide purification, polylactide synthesis, polymer finishing processing, waste disposal [8-9].

To obtain high molecular polylactide for medical products the lactide with minimal content of acidic impurities is required (water content less than 100 ppm, content of free lactic acid less than 50 ppm and pH from 0 to 1 mEq/kg) [10-12]. The presence of OLA has a negative effect on the polymerization reaction. This is due to the fact that the condensation of these substances results in water, which inhibits a polymerization reaction.

Purification of crude-lactide may be carried out by distillation, rectification, extraction, crystallization from the melt, recrystallization from the solvent, sorption, and other methods [8]. Lactide recrystallization from solvents is the most common method [13-14]. For purification of various optical lactide isomers the following substances are offered: aliphatic tertiary alcohols,

ketones, esters, aromatic hydrocarbon solvent and aliphatic hydrocarbon solvent having from 5 to 12 carbon atoms [15]; ethanol [16]; isopropanol, 1,2-dichloroethane, toluene [17]; t-amyl-alcohol, t-butylalcohol [18]; chloroform, butylethanoate, ethylethanoate and/or methylene-chloride [19]; toluene and ethylacetate washing [20]; 93% ethanol [21]; water and acetone [21]; methylisobutylketone [22]; diisopropyl ether [12], carbontetrachloride [23], ethylacetate or toluene, alcohols, ketones, and mixtures of them [24].

Also, for preparing D, L-Lactide from the mixture of D-Lactide and L-Lactide their joint recrystallization from toluene is used [25].

To develop the technology of lactide purification by recrystallization method the data on the qualitative and quantitative content of impurities in the crude-lactide, as well as solubility of lactide and basic impurities in various solvents are needed.

D and L-lactide solubility in ethanol, ethyl acetate, acetone, isopropanol, methanol and methylbenzene data, obtained by dynamic laser monitoring method in the temperature range of 278.15 - 338.15K, are known [26].

There are also the data on LA solubility in alcohols, ethers, ketones, aromatic and organo-chlorine hydrocarbons shown in Tab. 1 [27]. LA solubility (g/100 ml) was calculated from the patent data for ease of comparison with the results obtained in this work (Tab. 1).

There are also the data on solubility of crude-lactide, containing L-Lactide: 89.6%, Meso-lactide: 4.0%, LA monomer: 2.2%, LA dimer: 0.2, LA trimer: 0.2%, in some organic solvents, shown in Tab. 2 [28]. Lactide solubility (g/100 ml) was also calculated from the patent data.

Table 1. LA solubility at 20ºC

Solvent	Solubility, % wt	Solubility, g/100 mL	Solvent	Solubility, % wt	Solubility, g/100 mL
Ethanol	70.9	192	Ethyl acetate	39.9	60
1-Propanol	62.4	133	Chloroform	0.67	1
2-Propanol	63.4	136	2-Butanone	52.9	90
1-Butanol	54.5	97	Acetone	61.4	126
Toluene	0.11	0.1			

Table 2. Crude-lactide solubility at 23ºC

Solvent	Solubility, % wt.	Solubility, g/100 mL	Solvent	Solubility, wt.	Solubility, g/100 mL
Tert-butyl alcohol	5.6	5	Naphtha	0.1	0.1
Tert-Amyl alcohol	5.6	5	Diethyl ether	4.7	4
Methylethyl ketone	38.1	50	2,2,4-trimethyl-pentane	0.1	0.1
Ethylacetate	27.0	33	Toluene	7.7	7

2. Experimental

2.1. Materials

The following materials were used in the given work: 80% solution of L-LA produced by M.C.D. Import & Export Gmbh Germany, zinc oxide produced in Germany, solvents: ethyl acetate (at least 99.7 wt.%), butylacetate (not less than 98.5 wt.%), toluene, cumene, benzene, trichloroethane, carbon tetrachloride, ethanol, acetone, butanol, isopropanol, o-dichlorobenzene, bromobenzene, chlorobenzene, bromoethane. Solvents were not subjected to further purification.

2.2. Oligomer synthesis

Obtaining OLA with different molecular weight was carried out using a rotary vacuum evaporator "Heidolph" at 160°C, 20 - 30 mbar and with a reaction flask rotation speed 60 rev/min. 200 ml of LA was placed into a round bottom flask and solvent water was distilled under vacuum. After 1.5 hours the catalyst (zinc oxide) in amount of 1.5% mass of oligomer

was added into the reaction mixture and solvent and condensation water was distilled under the same conditions for another 2.5 - 3 hours under vacuum of 20 - 30 mbar.

2.3. Lactide synthesis

Lactide synthesis was performed using a standard vacuum distillation installation provided with an air condenser, an electromagnetic stirrer "IKA C-MAG HS 7" and a vacuum station (Vacuumbrand PC 3001 VARIO) at 5-10 mbar and 180-240°C.

2.4. Crude-lactide purification

Crude-lactide purification was carried out by recrystallization from ethyl acetate. Lactide drying was carried out at a 5-10 mTorr in freeze-drying installation (FreezeDryermodel № TFD8503).

2.5. Product analysis

The lactide melting point was determined using Melting Point M560. The substances solubility was determined by previously described methods [29-30]. Oligomer molecular weight was determined using gel permeation chromatography (AGILENT TECHN. 1200, calibrated with standard polystyrene samples).

3. Results and duscussions

When obtaining L-lactid by depolymerization of OLA the following substances, which release water during the reaction of polycondensation, are formed as major impurities: L-lactide (70÷90, wt.%), D-lactide (<1), LA (2÷10), water (0.1÷5), meso-lactide (3÷25), dimers (2÷10), trimers, tetramers and higher molecular weight linear LA oligomers [31-32]. Water prevents obtaining high molecular weight polymer.

Therefore, when crude-lactide recrystallization, all these impurities must be removed from the product, while minimizing the loss of lactide.

To select the solvents solubility of OLA with different molecular weights (Tab. 3 and Tab. 4) and of lactide with varying degrees of purity was determined. It will provide the use of the most effective solvents to obtain lactide with a high degree of purity.

Table 3. Solubility of OLA with molecular weight 690 g/mol

Solvent	Tempe-rature,°C	Solubility, (g/100mL)	Solvent	Tempe-rature,°C	Solubility, (g/100mL)
Butylacetate	-4	12±1	Cumene	20	6±1
Benzene	-4	4±1	Trichloromethane	20	9±1
Ethylacetate	-10	12±1	Carbon Tetrachloride	20	26±3
Cumene	-10	3±1	Ethylacetate	20	33±3
Benzene	20	49±5	Butylacetate	20	31±3

Table 4. Solubility of LA oligomer with molecular weight 1270 g/mol at 23°C

Solvent	Temperature,°C	Solubility, (g/100mL)
Ethanol	20-23	9±1
Acetone		25±3
Butylalcohol		10±1
Toluene		13±+1

The oligomer dissolved in those solvents for several minutes with stirring. Therefore, in this case, the oligomer hydrolysis reactions can be neglected. The findings suggest that the LA oligomer is readily soluble in aromatic compounds, ketones, and esters, and much worse in alcohols. As temperature increases, the solubility of the oligomer in the solvent increases as well.

The experimental data on crude-lactide solubility with a melting point of 94.4°C and pure lactide solubility with a melting point of 97-98°C are presented in Tab. 5 and Tab. 6, respectively.

The crude-lactide may contain a basic substance and impurities in various amounts and proportions according to the catalyst, preparation method, process parameters and feedstock

purity. Therefore, the intermediate product solubility data may vary significantly. The difference in data on crude-lactide and pure lactide solubility can be explained by this fact (Tab. 6). The solubility of pure lactide in ethylacetate is illustrated in Tab. 6 and crude-lactide in Tab. 2, respectively.

Table 5. Experimental data on crude-lactide solubility (t_{mp}=94-95°C) at 23°C

Solvent	Solubility, (g/100ml)
Ethanol	8±1
Butanol	8±1
Isopropanol	6±1
Carbon Tetrachloride	14±1
O-dichlorobenzene	8±1
Bromobenzene	14±1
Bromoethane	15±1

Table 6. Experimental data on lactide solubility (t_{mp}= 97-98°C) [33]

Solvent	Temperature,°C	Solubility, (g/100mL)
Ethylacetate	40	24±4
	23	21±2
	0	13±1
Butylacetate	23	15±2
	0	13±1
Vinylbutylether	40	10±1
	23	8±1
	0	7±1
Trichloromethane	23	57±9
	16	36±5

The lactide solubility in ethanol is many times less than the LA solubility, so this solvent is sometimes used for the primary removing of LA and oligomer [16, 21].

Dissolution of crude-lactide in water for a few minutes at 60 °C is recommended for meso-lactide removal from it [31]. Under these conditions, the rate of dissolution and hydrolysis of meso-lactide is much higher than of L-lactide, D-lactide, or D, L-lactide. To remove meso-lactide from L-lactide recrystallization from diisopropylether, tetrahydrofuran and 1,2-dimethoxy-ethane is also used [32]. Due to this process it is possible to reduce meso-lactide content in 3-4 times.

Besides, it should be taken into account that while heating crude-lactide with some solvents a racemization reaction can take place. In some cases, this process is undesirable. For example, it is recommended to use L-lactide as a raw material for medical products from polylactic acid with long biodegradation time [34].

4. Conclusion

The data on OLA and lactide solubility allow selecting a sequence of using the solvents for recrystallization according to the compound and impurities content in crude-lactide. This allows effective removing the impurities of LA or LA oligomer from crude-lactide and reducing lactide losses in the purification process.

The obtained data can be used to select a solvent for lactide crystals flushing, as well as to select solvents for the production of LA oligomer, lactide and polylactide using azeotropic distillation of water.

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Symbols

T – temperature, ºC *LA – lactic acid*
P – pressure, mbar, mtorr *OLA – lactic acid oligomer*

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