LIPID EMULSIONS (LE) AND AQUEOUS LECITHIN DISPERSIONS (WLD) AS PARENTERAL CARRIERS FOR POORLY SOLUBLE DRUGS

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INTRODUCTION

Many active substances are poorly water-soluble. In order to administer these drugs in the form of a solution (such a form is required e.g. for intravenous application) usually to the formulation co-solvents or artificial surfactants are added. These excipients, however can be in many cases substituted by biocompatible and biodegradable natural solubilizers – phospholipids and oils. These substances are used for years as excipients in submicron emulsions and dispersions intented for parenteral application.

AIM OF THE STUDY

The aim of the work was to prepare and characterize LE and WLD as potential parenteral carriers used for solubilization of two model, poorly soluble, drugs: carbamazepine and hydrocortisone. Additionally physical properties of both formulations without drugs were also analyzed.

CONCLUSIONS

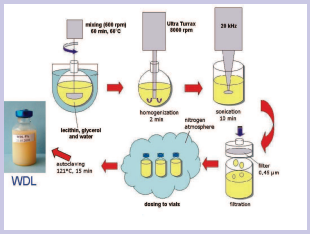
Physical tests indicated, that both LE and WLD fulfill the requirements of the carrier intended for parenteral application. It was also confirmed, that the solubility of carbamazepine and hydrocortisone in WDL or LE is higher comparing to water. WDL as well as LE can be used as ex tempore solvents for poorly soluble drugs intented for parenteral application.

EXPERIMENTAL METHODS

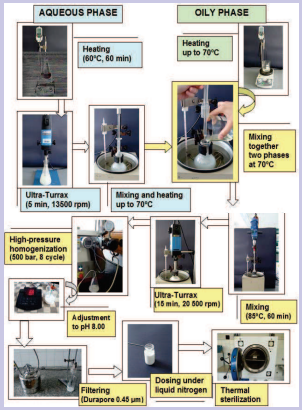
Composition of the dispersions

Type of dispersion		Soya-bean oil [%]	Egg lecithin [%]	Other excipients
WLD	WDL 5.0	-	5.0	Glycerol 2.5% NaOH Purified water
	WDL 10.0	-	10.0	
Lipid emulsion (LE)	LE 1.2	10.0	1.2	
	LE 2.4	10.0	2.4	
	LE 5.0	10.0	5.0	

WLD preparation



LE preparation



In order to analyze drugs solubility the access of hydrocortisone or carbamazepine was added to the formulations (WLD, LE and water) and the suspension was stirred 24h at room temperature using magnetic stirrer (500 rpm). Next suspensions were centrifugated and the concentrations of drugs was determined.

Physical properties of WLD and LE (without drugs) were analyzed using following methods:

- visual and microscopic observations,
- pH measurements,
- particles size was measured (oily droplets in LE and phospholipids patricles in WLD) using LD and PCS techniques.

Quantitative determination of hydrocortisone and carbamazepine in WLD and LE was performed using UV-spectrophotometry or HPLC methods (details in table below).

Drugs	HPLC method				UV-spectrophotometry	
	Chromatography column	Mobile phase	Analytical wave [nm]	Retention time [min]	$A^{1\%}_{1cm}$	Analytical wave [nm]
Carbamazepine	LiChrospher 100 RP-18 (250x4 mm, 5 µm)	Acetonitrile (28%)	237	11	424	285
Hydrocortisone		Acetonitrile : methanol: water (25:25:50 v/v)	254	6	443	242

RESULTS

Using described methods three types of formulations were obtained (Fig.1):

- LE - submicron emulsion (E 1.2, E 2.4 - oily droplet size below 1 µm)
- LE - traditional emulsion (E 5.0 – oily droplet size above 1 µm)
- WLD (5.0 and 10.0) with phospholipids particles about 2.2 µm.

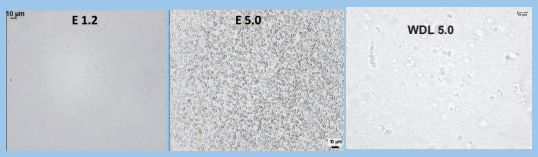


Figure 1. Microscopic observations of LE (E1.2 and E5.0) and WLD (bar 10 µm).

Submicron emulsions, which were characterized by size of oil droplets about 300 nm, were prepared using egg lecithin (1.2% and 2.4%). Despite the fact that emulsion with 5% of egg lecithin (E5.0) was not submicron type ($d_{0.9}$ 1.16 µm), this emulsion was stable (Fig. 2). The size of phospholipid particles in WLD was about 2.2 µm ($d_{0.5}$).

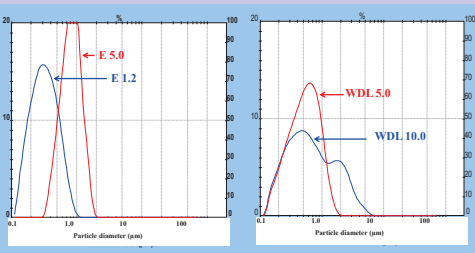


Figure 2. Size of oily droplet (in emulsions) and phospholipid particles (in WLD) in tested dispersions.

Solubility of drugs in dispersions

In all tested formulations the solubility of carbamazepine and hydrocortisone in WDL or LE was higher then in water. Solubility of hydrocortisone increased from 0.3 mg/ml (water) to 0.9 mg/ml (LE containing 1.2% of lecithin and 10% of the oil) and to 2 mg/ml (WLD containing 5% of egg-lecithin) Fig. 3. Also the solubility of carbamazepine in WDL was better than in LE, even if both formulations contained the same lecithin concentration (5%). It was also noticed that regardless of the type of carrier (LE or WLD) the increase in phospholipid concentration caused the increase in tested drug's solubility.

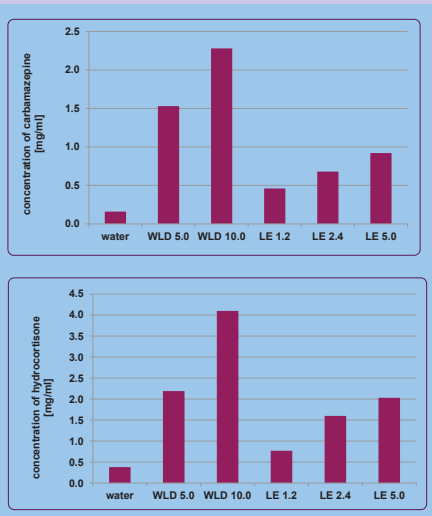


Figure 3. Solubility of carbamazepine and hydrocortisone in water, WDL and LE.

The study was supported by National Science Center (Cracow, Poland) grant NN 405 668440.