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Study on Drug Release from Oleogel Carriers

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1. Introduction

In the recent years, the research and development of gels and gel-forming polymers has started to develop enormously. The studies were mainly aimed at studying the gel structure of hydrogels and expanding their applications. Relatively few studies deal with oleogels as drug delivery systems and their potential for pharmaceutical technology. Organogels are thermoreversible, viscoelastic materials that can be formed using low molecular weight gelling aids (1). These are gelling agents which can even gel a surprisingly small percentage of the organic medium and / or water into which they are incorporated (2). The aim of the work was to study how different liquid lipids (gelling oils) affect the formed gel structure and drug release; to investigate the extent to which the non-steroidal anti-inflammatory drugs with different lipid solubilities used as model compounds can be released from the formed gels; to examine how the physical and rheological properties of the gels produced are affected by the active ingredients dispersed in them and why the use of oleogels may be more advantageous than hydrogels for some active ingredients.

2. Materials and methods

Castor, olive, flax, cod liver, paraffin, neutral (all Ph.Eur.X. quality) and wheat germ (from Herbárium 2000 Ltd.) oils were used to prepare the gels.

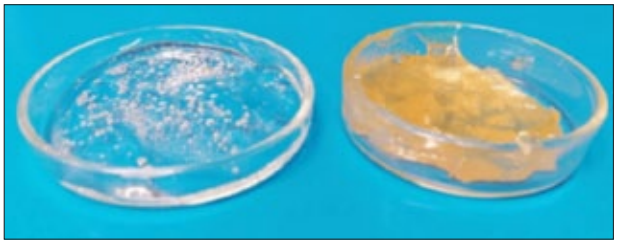

Figure 1 *Oleogels (neutral oil based gel (left), castor oil based gel (right))*

The gelling agent of choice was a low molecular weight compound, colloidal silica (Ph.Eur.X.), also known as aerosil. Colloidal silica is excellent for gelling vegetable oils. This oleogelator is capable of gelling in small amounts, the formulated gels were 7 w/w%. The model drugs were indomethacin and diclofenac-Na (both from Hungaropharma). The rate of drug release was examined by membrane diffusion method, and the gel was separated from the dissolution medium by an artificial membrane (Sartorius cellulose acetate filter, pore size: 0.2 μm). The rate of drug release can be examined in a properly thermostated (T=37°C) and circulating medium. The determination was performed spectrophotometrically (Spektromom 195D; $\lambda_{indomethacin}$=235 nm; $\lambda_{diclofenac\text{-}Na}$=276 nm). The Franz diffusion cell is suitable for modeling drug release and transdermal permeation. The determination was also performed spectrophotometrically. Viscosity was tested with a Malvern rotary viscometer.

3. Results

Of the two drugs, indomethacin, which had the higher lipid solubility, was the one that was most easily delivered by the formulated gels in the highest percentage of cases. Diclofenac-Na has also been shown to be suitable in the formulated gel compositions, however, the release was generally slower than that of indomethacin. In the spreading studies, it was found that the spreading of the gels containing the active ingredient was smaller. This was also confirmed by viscometer studies. The dispersion of gels containing indomethacin was most similar to that of "empty" gels. This is due to the lipid solubility of indomethacin. We also selected the gel composition that releases diclofenac-Na the fastest and compared it with commercially available hydrogels containing diclofenac-Na. As a result, diclofenac-Na is much slower and more continuously released from oleogels than from hydrogels.

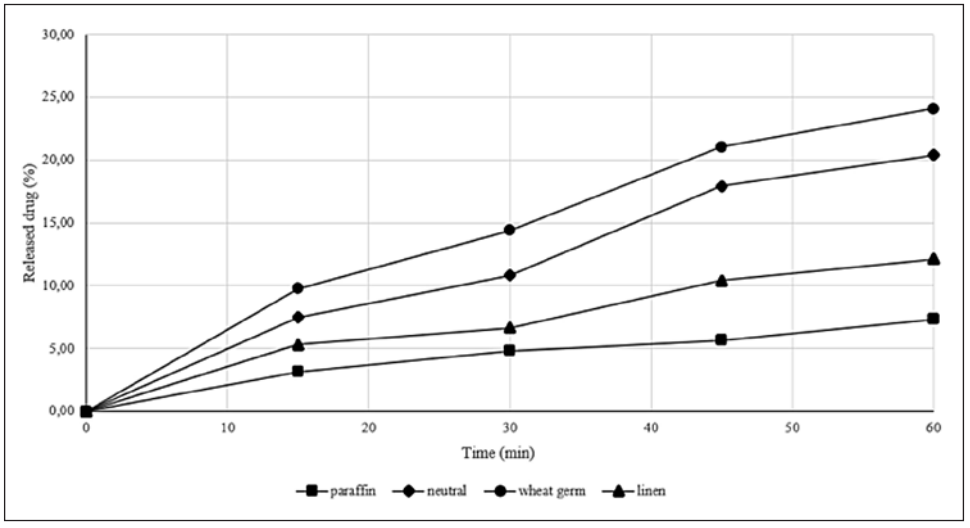

Figure 2 *Release profile of diclofenac-Na loaded oleogels*

Table I *Released drug (%) from various carriers (C:castor; P: paraffin; N:neutral)*

time (min)	Diclofenac-Na			Indomethacin		
	C	P	N	C	P	N
0	0.00	0.00	0.00	0.00	0.00	0.00
15	1.36	3.14	7.46	2.24	0.64	8.22
30	2.67	4.82	10.80	3.73	3.65	10.44
45	3.34	5.66	17.91	5.19	10.52	16.23
60	4.85	7.34	20.37	5.89	18.87	20.04

Table II *Released diclofenac-Na (%) from hydrogels and oleogels*

Time (min)	Hydrogels			Oleogels			
	Diclofenac Dolo	Carbomera 3%	Carbomera 5%	wheat germ	neutral	linen	paraffin
15	19.81	8.74	8.62	9.74	7.46	5.32	3.14
30	28.75	19.82	18.09	14.39	10.79	6.63	4.82
45	47.62	32.33	23.42	21.04	17.92	10.41	5.66
60	57.45	38.73	29.85	24.07	20.37	12.09	7.34

4. Conclusions

In evaluating the studies, it was concluded that oleogels of this or a similar composition may be suitable for topical use, for example as a local anti-inflammatory or analgesic. The Franz cell and membrane diffusion studies have shown that the release of diclofenac-Na and indomethacin is much more continous and slower than that of hydrogels containing the same amount of active substance, so a longer, more prolonged effect can be achieved with them. Their permeability skills were adequate. There was a significant difference in the drug release of some oleogels, due to the use of different vegetable, animal or synthetic oils and their different properties. In general, the release of the indomethacin was faster than the release of the diclofenac. This is due to the higher lipid solubility of indomethacin, in which case the rate-determining step may be the diffusion of the drug. These experiments have also shown that oleogel carriers can be suitable for both lipophilic and hydrophilic drugs, although the release of hydrophilic drugs may be slower(3). The active ingredients may be located in different ways in the gel skeletons of gels made from different oils, for physical and chemical reasons. From this it can be concluded that by modifying the gel compositions, different drug delivery systems can be produced. Overall, gels of this type may be suitable for topical use due to their rheological properties and drug-carrying ability.

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