



# IJPPR

INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH  
An official Publication of Human Journals

ISSN 2349-7203



Human Journals

**Review Article**

October 2017 Vol.:10, Issue:3

© All rights are reserved by SHOWKAT HUSSAIN SOFI et al.

## Gelucire: A Versatile Formulation Excipient



**IJPPR**  
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH  
An official Publication of Human Journals

ISSN 2349-7203



**SHOWKAT HUSSAIN SOFI\*, PAHUJA SONIA**

*Department of Pharmaceutical Sciences, Swami  
Vivekanand College of Pharmacy, Patiala 146001,  
Punjab, India*

**Submission:** 19 September 2017  
**Accepted:** 29 September 2017  
**Published:** 30 October 2017

**Keywords:** Gelucire, Triglycerides, Hydrophilic-Lipophilic Balance, Hard Fat.

### ABSTRACT

Of late, Gelucire has been the focus of pharmaceutical research, owing to its numerous advantages over conventional lipids. Chemically, Gelucire can be catalogued as the group of vehicles acquired from blends of mono, di- and triglycerides with PEG esters of unsaturated fats. The polyglycolic glycol esters like Gelucires which is available in varied grades offers multifaceted applications in immediate and controlled release drug delivery systems. The current review attempts to provide an updated and exhaustive insight into the published literature reports vouching for the versatility of Gelucire as a vehicle in formulation development. Conclusively, the intention is to provide scope for future developments of successful formulations using this novel lipid.



HUMAN JOURNALS

[www.ijppr.humanjournals.com](http://www.ijppr.humanjournals.com)

## INTRODUCTION

For more than two decades, considerable use of polymeric materials to deliver bioactive agents has attracted attention of various investigators throughout the scientific community. Polymer chemists, chemical engineers along with pharmaceutical scientists are extensively engaged in bringing out the design and development of various controlled drug delivery systems.<sup>1</sup>Invariably, the polymers which are employed to formulate floating drug delivery systems are designed/tailored to provide drug delivery to specific region in the GIT.<sup>2</sup>Numerous materials have been studied extensively in the design of drug delivery systems and one of the favored excipients is Gelucire.<sup>3</sup>

Recently, much attention has been focused on the use of fats and fatty acid as carriers in drug delivery systems.<sup>4,5,6</sup> These include coconut oil, olive oil, soyabean oil, palmitic acid, behenic acid and stearic acid. The amphiphilic lipid glyceryl monooleate has been used for the design of floating matrix system.<sup>7</sup> Gelucires are mixtures of glyceride-based materials and esters of polyethylene glycol (PEG) which can be used in the preparation of controlled release drug dosage forms. These polymeric materials contain mixtures of mono-, di- and triglycerides with esters of polyethylene glycol (PEG). The presence of these components offers hydrophobic and hydrophilic natures to the dosage form. The nature and proportion of these components can control the hydrophobicity and drug release properties in the drug dosage forms.<sup>8</sup> Gelucires are inert, semi-solid, waxy, amphiphilic excipients with surface-active properties that spontaneously form a fine dispersion or emulsion upon exposure to water.<sup>9</sup> They are available in different types. The different types of Gelucires can be identified by two numbers/values. Among these two numbers, first number indicate melting point of the base (varies from 33°C-65°C) and the second number indicates HLB value of the proportion of water-soluble, parts to fat-soluble in each Gelucire (varies from 1 to 14). In the designation of its name, for example, Gelucire 54/02, 54 indicates melting point while 02 indicates its HLB value.<sup>10</sup>

The wide range of the melting point and the proportion of hydrophilic-lipophilic components in Gelucires make them widely applicable in the preparation of different types of dosage forms, especially in the preparation of both fast and slow release formulations.<sup>11</sup> The polyglycolized glycol esters like Gelucires are reported to reduce erratic bioavailability of poorly water soluble drugs.<sup>12</sup> Gelucires are among the several carriers which have been employed in preparing solid dispersions. They are enormously used in controlled-release

matrices in order to enhance the physicochemical properties of drug. Gelucire 44/14 possesses surfactant and self-emulsifying properties which can be used as meltable binder by melt granulation of poorly water-soluble active substances. In contact with aqueous fluids it forms a fine emulsion which solubilizes the active substances and hence increases its oral bioavailability.<sup>13</sup> Gelucires with low HLB values in lipid matrices can decrease the dissolution rate of the drugs from the lipid matrices,<sup>14,15</sup> whereas Gelucires with high HLB values can accelerate the release rate of the drugs from the lipid matrices.<sup>16,17</sup> Gelucire enhances the drug release process by forming hydrogen bonds with the active substance, leading to the formation of stable solids of amorphous drug in microparticles.<sup>18,19</sup> The lipidic materials such as Gelucire are considered as an alternative to other polymers employed in sustained release formulations because of following advantages<sup>20</sup> such as:

- i) Low melt viscosity, thus obviating the need of organic solvents for solubilisation.
- ii) Absence of toxic impurities such as residual monomer catalysts and initiators.
- iii) Potential biocompatibility and biodegradability.
- iv) Prevention of gastric irritation by forming a coat around the gastric irritant drug.

## PHYSICOCHEMICAL PROPERTIES

Each component of Gelucire presents different affinity for water and act as surfactant and co-surfactant. Di- and triglycerides are lipophilic in nature. Certain Gelucires are produced by the reaction of hydrogenated palm kernel oil and polyethylene glycol, PEG-33 (Gelucire 44/14). It contains PEG-33 esters, glycerides, unreacted PEG-33 and a small amount of glycerol.<sup>10</sup> The hydrophilic property of the polymer is quite useful in the dissolution enhancement as well as in control release formulations.<sup>13</sup>

Owing to the extreme hydrophilicity and low density, Gelucire 50/13 may be considered an appropriate carrier for designing fast release floating drug delivery system. On the other hand, due to the extreme hydrophobicity and low density, Gelucire 39/01 and 43/01 are considered as appropriate carriers for designing sustained release floating drug delivery systems. Gelucires containing only glycerides or a mixture of glycerides and PEG esters (Gelucire 39/01, 43/01) are used in the preparation of sustained release formulations.

A vast number of Gelucires containing triglycerides are currently available. Specific examples of Gelucires are:

- Gelucire 44/14 (saturated polyglycolized glycerides)
- Gelucire 50/13 (saturated polyglycolized glycerides)
- Gelucire 39/01 (semi-synthetic glycerides)
- Gelucire 53/10 (saturated polyglycolized glycerides)
- Gelucire 33/01 (semi-synthetic triglycerides of C<sub>8</sub>-C<sub>18</sub> saturated fatty acids)
- Other Gelucires, such as 37/06, 43/01, 35/10, 37/02, 46/07, 48/09, 50/02, 62/05, etc.

The main grades of Gelucire and their properties are described below:

#### **Gelucire 43/01 (Hard fat EP/NF/JPE)**

Gelucire 43/01 is a hydrophobic lipid with an HLB value of 1 and melting point of 43°C. It is a blend of saturated triglycerides of different fatty acids, viz., C<sub>8</sub> - 3%, C<sub>10</sub> - 2%, C<sub>12</sub> - 29%, C<sub>14</sub> - 2%, C<sub>16</sub> - 17%, and C<sub>18</sub> - 36%.<sup>21</sup> Gelucire 43/01 is used in lipid matrix formulations for sustained release effect. It is also used in combination with other grades of Gelucire to modify drug release for oral delivery. In dermal delivery, it can be used as a consistency agent for mineral phase in lipophilic ointment.

#### **Key Features<sup>22</sup>**

##### **Oral**

- i) It is protective carrier for API sensitive to oxidation, humidity or light.
- ii) Its high melting point lipid can be used in modified release dosage forms (lipid matrix in capsules, floating granules).
- iii) It is used as a lipid binder in melt techniques where the physicochemical properties and plasticity of the lipid agglomerate provides high resistance to fracture, useful for flash melt and chewable tablets.

## Topical

- i) Consistency agent (thickener) for topical formulations.
- ii) Safety of use is supported by toxicological data and food additive status.

Table 1 gives the characterization parameters of Gelucire 43/01 as:

**Table 1: Characterization Parameters of Gelucire 43/01**

Physical Form	Hydrophilic-Lipophilic Balance (HLB)	Field of Use	Administration Route
Semi-solid Block	1	Human pharmaceutical products, veterinary products excluding food producing animals(EU)	Oral, Topical

## Formulation techniques and dosage forms

- i) Use in melt processing techniques: melt granulation (thermoplastic pelletization), hot melt coating and melt extrusion for capsule filling, tableting, sachets etc.
- ii) Suitable for hard gelatin capsule molding.
- iii) Use in topical emulsions and microemulsions.

## Gelucire 44/14 (Lauroyl macrogol-32 glycerides EP)

Other names: Lauroyl polyoxyl-32 glycerides NF,

LauroylPolyoxylglycerides (FDA IIG)

Gelucire 44/14 is a semi-solid excipient among the group of Gelucires. It is characterized by two numbers, the first indicates a nominal melting point of 44°C and the second to the hydrophilic-lipophilic balance (HLB) value of 14.<sup>23</sup> This number reflects the proportion of water soluble to lipid soluble moieties in each material.<sup>8</sup> Gelucire® 44/14 combines interesting properties because of its unique composition of surfactants (mono- and diesters) of polyethylene glycol, cosurfactants (monoglycerides), and oily phase (di- and triglycerides).<sup>24</sup> Gelucire 44/14 is obtained by polyglycolysis of hydrogenated palm kernel oil with

PolyethyleneGlycol 1500. Its composition is a mixture of mono-, di-, and triglycerides - 20%, Mono- and di-fatty acid esters of PEG 1500-72% and Free PEG 1500-8%.<sup>13</sup> The fatty acid distribution of Gelucire 44/14 is specified in Table 2:

**Table 2: Fatty Acid Distribution of Gelucire 44/14**

Caprylic Acid (C8)	Capric Acid (C10)	Lauric Acid (C12)	Myristic Acid (C14)	Palmitic Acid (C16)	Stearic Acid (C18)
4-10%	3-9%	40-50%	14-24%	4-14%	5-15%

**Key Features<sup>22</sup>**

- i) A non-ionic water dispersible surfactant composed of well-characterized PEG-esters, a small glyceride fraction and free PEG.
- ii) Able to self-emulsify on contact with aqueous media forming a fine dispersion i.e. micro-emulsion (SMEDDS).
- iii) Solubilizer and wetting agent: surface active power improves the solubility and wettability of active pharmaceutical ingredients *in-vitro* and *in-vivo*.
- iv) Bioavailability enhancement associated with improved in vivo drug solubilization which facilitates absorption.
- v) Good thermo-plasticity for use as a binder in melt processes, associated with rapid formation of stable crystalline phase.
- vi) Safety of use is supported by extensive toxicological evaluations and precedence of use in approved pharmaceutical products.

The characterization parameters of Gelucire 44/14 are given in Table 3 below:

**Table 3: Characterization Parameters of Gelucire 44/14**

<b>Physical Form</b>	<b>Hydrophilic-Lipophilic Balance (HLB)</b>	<b>Field of use</b>	<b>Administration Route</b>
Semi-solid block	11	Human pharmaceutical products, veterinary products excluding food producing animals (EU)	Oral

**Formulation techniques and dosage forms**

- i) Suitable for use in melt processing techniques: melt granulation (thermoplastic pelletization) and melt extrusion techniques for capsule filling, tableting, sachets etc.
- ii) Suitable for hard gelatin capsule molding.
- iii) Suitable for adsorption onto neutral carrier powders for use in tablets, capsule filling and sachets.

**Gelucire 50/13 (Stearoyl macrogol-32 glycerides EP)**

**Other Names:** Stearoyl polyoxyl-32 glycerides NF

Stearoyl Polyoxylglycerides (FDA IIG)

Gelucire 50/13 is a mixture of glycerides (mainly C16/18) and mono and diesters of PEG 1500.<sup>25</sup> Gelucire 50/13 is obtained by PEGylation of stearoyl glycerides and has considerably higher molecular volume as compared to Gelucire 44/14.<sup>26</sup>

**Key Features<sup>22</sup>**

- i) A non-ionic, water dispersible surfactant composed of well-characterized PEG-esters, a small glyceride fraction and free PEG.
- ii) Able to self-emulsify on contact with aqueous media forming a fine dispersion i.e., micro-emulsion (SMEDDS).
- iii) Solubilizer/wetting agent: surface active power improves the solubility and wettability of active pharmaceutical ingredients *in-vitro* and *in-vivo*.

- iv) Bioavailability enhancer: improved *in-vivo* drug solubilization facilitates absorption.
- v) Good thermoplasticity for use as a binder in melt processes.
- vi) Safety of use is supported by toxicological data and precedence of use in approved pharmaceutical products.

Table 4 gives the important characterization parameters of Gelucire 50/13 as below:

**Table 4: Characterization Parameters of Gelucire 50/13**

Physical Form	Hydrophilic-Lipophilic Balance (HLB)	Field of Use	Administration Route
Semi-solid block	11	Human pharmaceutical products, veterinary products excluding food producing animals (EU)	Oral

#### Formulation techniques and dosage forms

- i) Used in melt processing techniques: melt granulation (thermoplastic pelletization) and melt extrusion techniques for capsule filling, tableting, sachets etc.
- ii) Suitable for hard gelatin capsule molding.
- iii) Suitable for adsorption onto neutral carrier powders for use in tablets, capsule filling and sachets.

#### Gelucire 39/01

Gelucire 39/01 comprises a mixture of hemi-synthetic glycerides of different fatty acids melting at 39°C. Extreme hydrophobicity of Gelucire 39/01 is attributed to the absence of PGE esters, which in turn provides release-retarding ability.<sup>27</sup> Gelucire 39/01 is lipophilic carrier chemically consisted of glycerol esters of saturated C12-C18 fatty acids. The properties and uses of Gelucire 39/01 are indicated in Table 5:



**Table 5: Characterization Parameters of Gelucire 39/01<sup>22</sup>**

<b>Physical Appearance</b>	Waxy Solid
<b>Melting Point</b>	39°C
<b>HLB</b>	1
<b>Regulatory Status</b>	JSFA, EP, USP/NF, JPED approved; DMF no. 6028
<b>Uses</b>	Excipient, carrier, vehicle, consistency agent, fattening agent for pharmaceutical hard gelatin capsules, low density products, low dose or toxic drugs, oily phase ointment, carrier protecting active ingredient from light, moisture and oxidation.
<b>Description</b>	Gelucire 39/01 is a carrier for oral formulations and specifically for hard or soft gelatin dosage forms. Gelucire 39/01 can protect the active pharmaceutical ingredient from light, moisture and oxidation, and can be used as an oily vehicle in Self Emulsifying Lipidic Formulations (Self type SEDDS and SMEDDS).

### **Characterization of Gelucire containing formulations**

In order to characterize Gelucire containing formulations, several parameters can be studied including the physical stability of drug in the matrix systems. Moreover, crystallinity and polymorphic and/or pseudo-polymorphic form of drug in a matrix containing Gelucire can be assessed by differential scanning calorimetry (DSC) and powder X-ray diffractometry (PXRD). Diffuse reflectance infrared fourier transform spectroscopy (DRIFTS) can also be employed to identify the nature of interactions between drug and the constituents of the polymeric matrix. However, several other techniques such as hot stage microscopy (HSM), hot stage polarizing microscopy (HSPM), scanning electron microscopy (SEM), and saturation solubility of formulation are available by which Gelucire containing formulations can be analyzed.<sup>10</sup>

## RECENT RESEARCH ENDEAVOURS

Several researchers have utilized Gelucires as a carrier in design of controlled release matrices.<sup>28</sup> The controlled release drug delivery system of salbutamol,<sup>29</sup> oxprenolol,<sup>30</sup> lithium sulphate, benzonatate,<sup>31</sup> quinidinegluconate and theophylline<sup>32</sup> have been formulated using Gelucire. It has been reported to be utilized for improving the physicochemical properties of the drug. While the hydrophilic property of Gelucire is normally useful in the dissolution enhancement, the hydrophobic variety is used in the design of novel controlled release products. The Gelucire 50/13 has been used to enhance drug release profiles for poorly soluble drugs such as nifedipine, diclofenac and praziquantel.<sup>33</sup>

In addition, it has been widely employed to enhance the oral bioavailability of poorly water-soluble drugs. These drugs include the antiviral agent UC781,<sup>34,35</sup> the antimalarial drug halofantrine,<sup>36</sup> the HIV protease inhibitor DMP 323<sup>37</sup> and theophylline.<sup>38</sup> There are reports citing its use in the oral formulation of nicotine.<sup>39</sup> Apart from these, a number of studies have reported the use of Gelucires in drug-loaded spheres<sup>40</sup> as a compressed tablet dosage form.<sup>41</sup> Gelucires have also been used as meltable binders because they present broad melting ranges that are particularly adapted for this kind of process. The progressive melting of the binder allows control of the process and the selection of the granule's size. Table 6 mentions the research endeavors undertaken by several investigators globally exploiting Gelucire as a potential carrier in formulating the diverse dosage forms.

**Table 6: Succinct Literature Citations of Gelucire as Formulation Carrier**

	Drug(s)	Gelucire Grade	Other Polymers	Technique	Remarks	Reference
<b>SOLID DISPERSIONS</b>	Albendazole	50/13	PEG 15000	Fusion Method	Substantial enhancement of dissolution performance	<sup>42</sup> de-los Santos <i>et al.</i> , 2017
	Exemestane	44/14	Vitamin E TGPS, Calcium Silicate	Solvent Evaporation	Improved permeability, solubility and dissolution	<sup>43</sup> Eedara <i>et al.</i> , 2016
	Fenofibrate	50/13	CO <sub>2</sub> , Acetonitrile	Melt Mixing/	Improved dissolution profile	<sup>44</sup> Pestieau <i>et al.</i> ,

				Freeze Drying		2015
	Valsartan	50/13	Pluronic F68, PEG, Magnesium Stearate	Melt Dispersion	Complete drug release in 30 min	<sup>45</sup> Chella <i>et al.</i> , 2014
	Fexofenadine HCl	44/14	Vitamin E TPGS	Melt Method	Improved oral bioavailability with enhanced solubility and permeability	<sup>46</sup> Eedara <i>et al.</i> , 2013
	Lycopene	44/14	Cremophor RH 40, Lecithin	Solvent Evaporation	Enhanced oral bioavailability	<sup>47</sup> Faisal <i>et al.</i> , 2013
	Progesterone	44/14	PEG (400, 4000) Vitamin E TGPS, Miglyol 812	Solvent Evaporation	Improvement in transdermal permeation over 24 h	<sup>48</sup> Falconer <i>et al.</i> , 2013
	Sirolimus	50/13	HPMC, PVP K30, PVP VA64, Poloxamer 407	Solvent Evaporation	Enhanced <i>in-vivo</i> oral absorption, enhanced bioavailability.	<sup>49</sup> Kim <i>et al.</i> , 2013
	Glibenclamide	50/13	PEG (200, 400, 4000, 6000)	Melt Granulation	Buoyancy > 11 h, improved solubility and dissolution	<sup>50</sup> Upadhyay <i>et al.</i> , 2012
	Candesartan Cilexetil	50/13	PEG-6000, Hydroxypropyl $\beta$ -CD, Poloxamer	Melt agglomeration and Solvent Evaporation	Enhancement of solubility and permeability	<sup>51</sup> M Shaikh <i>et al.</i> , 2011
	Raloxifene HCl	50/13	Succinic acid, Adipic acid, PEG, Tetrabutyltitana te	Melt Mixing	Sustained release obtained from Gelucire formulations	<sup>52</sup> Bikiaris <i>et al.</i> , 2009
<b>FLOATIN</b>	Risperidone	44/14, 50/13	HPMC K100M, Polyox WSR 301	Direct Compression	Better bioavailability, Gastric retention time > 6 h	<sup>53</sup> Babu and Ramana,

						2016
	MoxifloxacinH Cl	44/14	HPMC, POLYOX, Carnuba wax	Direct Compression	Satisfactory sustained release, Floating time > 12 h	<sup>54</sup> Arzaa <i>et al.</i> , 2016
	Cefuroxime Axetil	50/13, 43/01	Neusilin US2	Melt Granulation	Inhibition of E. Coli growth up to 12 h, Improved bioavailability	<sup>55</sup> Jammula <i>et al.</i> , 2015
	Metronidazole	39/01	Carmacel P- (CC), Methocel K15M CR	Melt Granulation and Compression	Gelucire 39/01 proved as efficient carrier for design of FDDS	<sup>56</sup> Juárez- Soberanez <i>et al.</i> , 2011
	Famotidine	43/01	HPMC K4M, NaHCO <sub>3</sub> , Magnesium Stearate	Direct Compression	Buoyancy <12 h, zero order release kinetics with non-fickian diffusion	<sup>57</sup> Patel <i>et al.</i> , 2011
	Nifedipine	43/01, 53/14	HPMC K4M	Wet Granulation	Controlled release of drug for more than 12 h, First order release	<sup>58</sup> Ramesh <i>et al.</i> , 2011
<b>LIPID FLOATING CAPSULES</b>	Risedronate Sodium	50/13	HPMC, POLYOX (WSR 303)	Wet Granulation	Improved physical characters and <i>in- vitro</i> release	<sup>59</sup> Bhikshap athi <i>et al.</i> , 2015
	Aceclofenac	44/14, 50/13, 33/01, 43/01	Aerosil 200, PEG (4000, 6000)	Melt Fusion	Significant enhancement in activity (p < 0.01)	<sup>60</sup> Kalpna <i>et al.</i> , 2014
	Carbamazepine	44/14	Citric Acid, NaHCO <sub>3</sub> , Avicel PH-102	Melt Granulation/ Spray Drying	Nearly 100% drug release obtained within 10 min dissolution time	<sup>9</sup> da Fonseca Antunes <i>et al.</i> , 2013
<b>SOLID</b>	Darunavir	43/01	Pecirol ATO5, Glyceryl caprylate	Hot Homogeniza tion	Max. Rel <sub>12h</sub> =80- 84%, Enhanced permeability	<sup>61</sup> Bhalekar <i>et al.</i> , 2017
	Methotrexate	50/13	Transcutol P, Phospholipon S	Hot Micro- emulsion	Suppression of the production of local and migratory	<sup>62</sup> Garg <i>et al.</i> , 2016

					regulatory T cells	
	Sodium Alendronate	44/14	Compritol, Cremophar,	Hot Homogenization	Improved solubility and wettability	<sup>63</sup> Ochiuz <i>et al.</i> , 2016
	Temozolomide	44/14	Labrafil, Labrasol, Labrafac, Capmul	High Pressure Homogenization	EE = 81.64±3.71%, Zeta potential = 15.21± 3.11 mV	<sup>64</sup> Khan <i>et al.</i> , 2016
	Curcumin	39/01, 50/13	Compritol 888 ATO, Poloxamer, PEG400	Hot Homogenization	SLP's with a high drug loading capacity and chemical stability obtained	<sup>65</sup> Hazzah <i>et al.</i> , 2015
	Dimethyl Dioctadecyl Ammonium bromide	44/14	Sepharose, Sorbitan, Phosphate buffer	Emulsification	Potential gene delivery systems obtained	<sup>66</sup> Oyewumi <i>et al.</i> , 2015
	Ketoprofen	43/01, 50/13	Peceol, CO <sub>2</sub> , Ethanol	High Pressure Precipitation	Structured solid lipid carriers successfully produced	<sup>67</sup> Gonsalves <i>et al.</i> , 2015
	Naproxen	44/14	Maltodextrin, Peceol, Maltodextrin	Spray Drying	Increased dissolution rates	<sup>68</sup> Čerpnjak <i>et al.</i> , 2015
	Gallium Acetyl-acetate	44/14, 53/13	Cetyl alcohol, Gallium chloride, Sephadex	Emulsification	Enhancement of anti-tumor activity, Minimum exposure to healthy tissues	<sup>69</sup> Wehrung <i>et al.</i> , 2013
	Docetaxel	44/14	Tween 80, Sephadex (G75, G25), Triton X-100	Melt Emulsification	Gelucire played influential role in drug release by facilitating diffusion from nanoparticles	<sup>70</sup> Wehrung <i>et al.</i> , 2012
	Repaglinide/ Celecoxib/ Triclosan	50/13	Precirol ATO 5, Compritol ATO 888, Capryol 90	Emulsification	Gelucire 50/13 acted as novel stabilizer	<sup>71</sup> Date <i>et al.</i> , 2011
SE	Glibenclamide	50/13,	Myverol,	Spray	Self dispersibility in	<sup>72</sup> Albertini

		44/14	Poloxamer, Cremophar	Congeaing	60 min, Micelle dimensions = 360nm	<i>et al.</i> , 2014
	Atorvastatin	44/14	Capryol, Transcutol Propylene Glycol	Melt Solidificatio n	Gelucire 44/14 presented higher affinity for lipophilic excipients	<sup>73</sup> Breitkrei tz <i>et al.</i> , 2013
	Fenofibrate	44/14	TPGS 1000, PEG 6000, Labrafil M 1944	Melt Solidificatio n	90-100% dissolution in 60 min, 20 fold increase in dissolution in SGF (pH 1.2)	<sup>74</sup> Kanaujia <i>et al.</i> , 2013
FLOATING MATRICES	Metoprolol Succinate	43/01, 44/14	-	Melt Solidificatio n	Floating duration > 12h	<sup>75</sup> Siripura m <i>et al.</i> , 2010
	RisedronateSod ium	43/01	Caprol PGE- 860, Compritol 888 ATO, Precirol,	Melt Solidificatio n/Melt Granulation	Gelucire 43/01 proved as an appropriate carrier for SR formulations	<sup>27</sup> Chauhan <i>et al.</i> , 2005
	Residronate Sodium	39/01	Methocel, HPMC	Melt Solidificatio n	Gelucire 39/01 proved as an appropriate carrier for SR formulations	<sup>76</sup> Chauhan <i>et al.</i> , 2004
MISCELLANEOUS	Metronidazole/ Norfloxacin	39/01	Sodium Alginate, Calcium carbonate	Extrusion Spheronizati on	Drug release extended upto 18 h	<sup>77</sup> Soni <i>et</i> <i>al.</i> , 2017
	Risperidone	43/01, 44/14, 50/13	Geleol, Compritol 888 ATO	Emulsion Solvent Diffusion	Promising <i>in-vitro</i> release with buoyancy up to 95.93% for 12 h	<sup>78</sup> Ammar <i>et al.</i> , 2016
	Furosemide	43/01	NaOH Pellets, KH <sub>2</sub> PO <sub>4</sub>	Melt Granulation	Zero order release pattern, Gelucire 43/01 proved as an effective carrier	<sup>79</sup> Kumar <i>et</i> <i>al.</i> , 2016
	Famotidine	43/01	Chitosan, Sodium	Emulsificati on Gelation	Gel strength increased with	<sup>80</sup> Tiwari <i>et</i> <i>al.</i> , 2015

		alginate, CaCO <sub>3</sub>		polymer amount	
Metformin Hydrochloride	39/01, 43/01, 50/13	PEG, Glyciphage	Melt Granulation	Increased bioavailability confirmed by IVIVC studies	<sup>81</sup> Upadhyay <i>et al.</i> , 2014
Piroxicam	39/01	Sodium Alginate	Emulsion Gelation	Increased analgesic / anti-inflammatory response	<sup>82</sup> Saxena <i>et al.</i> , 2013
DrotaverineHCl	43/01	Sodium Alginate, Span 80, Triethyl Citrate, PEG 400	Emulsion Gelation	Gelucire 43/01 based beads provided extended drug release	<sup>83</sup> Adel and Elkasabgy, 2013
Curcumin	44/14	PEG 400, Rhodamine 6 G, Citric Acid	Granulation	Lipid based oral formulations of Curcumin obtained with Gelucire 44/14	<sup>84</sup> Pawar <i>et al.</i> , 2012
Repaglinide	43/01	Ethyl Cellulose, β-CD, HP-βCD	Melt Granulation	Extended drug release up to 12 h following zero order	<sup>85</sup> Rao <i>et al.</i> , 2011
Diltiazem HCl	43/01	Glyceryl monostearate, Methocel K4M, Ethocel	Melt Granulation	Gelucire 39/01 proved as an appropriate carrier for multi-unit FDDS	<sup>86</sup> Shimpi <i>et al.</i> , 2004

Thus, the tabulated illustrations vouch for the unambiguous suitability of Gelucire as an effective carrier for delivery of a wide variety of active pharmaceutical ingredients.

## CONCLUSION

The recent developments connote to apt utilization of Gelucire and further scope of improvisation in the arena of Gelucire mediated drug delivery systems. Gelucire facilitated drug delivery technology has emerged as an efficient approach for enhancing the bioavailability and controlled delivery of numerous therapeutic moieties. Outstanding scientific progress has been made, demonstrating the potential applications of Gelucire in various formulation approaches. Gelucire has been successfully utilized by many

investigators globally in the development of drug delivery systems. These lipidic carriers have emerged as promising and efficacious agents with myriad of desired characteristics for effective drug delivery. It is further anticipated that the use of Gelucire as an indomitable excipient will expand the scope of new drug delivery systems in the near future.

## REFERENCES

1. Murthy RSR. Biodegradable polymers: Controlled and novel drug delivery. New Delhi: CBS Publishers & Distributors. 1997;1:27-51.
2. Beneke CE, Viljoen AM, Hamman JH. Polymeric plant-derived excipients in drug delivery. *Molecules*. 2009;14:2602-2620.
3. Jain S, Jain NK. Pharmaceutical product development: Polymers in pharmaceutical sciences, CBS Publishers, New Delhi. 2006;01:585-591.
4. Hauss DJ. Oral lipid-based formulations. *Adv Drug Deliv Rev*. 2007;59:667-676.
5. Jannin V, Musakhanian J, Marchaud D. Approaches for the development of solid and semi-solid lipid-based formulations. *Adv Drug Deliv Rev*. 2008;60:734-746.
6. Singh S, Chakraborty S, Shukla D, Mishra B. Lipid - An emerging platform for oral delivery of drugs with poor bioavailability. *Eur J Pharm Biopharm*. 2009;73:1-15.
7. Paradkar A, Shah MH, Ketkar A, Mahadi, KR. Effect of drug solubility and different excipients on floating behaviour and release from glyceryl monooleate matrices. *Int J Pharm*. 2007;272:151-160.
8. Craig DQM. The use of glycerides as controlled release matrices. In: Excipients and delivery systems for pharmaceutical formulations. London R Soc Chem. 1995;148-171.
9. da Fonseca Antunes AB, De Geest BG, Vervaet C, Remon JP. Gelucire 44/14 based immediate release formulations for poorly water-soluble drugs. *Drug Dev. IndPharm*. 2013;39:791-798.
10. Pahwa R, Kumar S, Saini N, Kumar V. Gelucire mediated gastric floating drug delivery systems. *PharmLett*. 2012;4:1038-1043.
11. Upadhyay P, Pandit JK, Wahi AK. Gelucire: an alternative formulation technological tool for both sustained and fast release of drugs in treating diabetes mellitus type II disease. *J SciInd Res*. 2013;72:776-780.
12. Pozzi F, Longo A, Lazzarini C, Carezzi A. Formulations of Ubidecarenone with improved bioavailability. *Eur J Pharm Biopharm*. 1991;37:243-246.
13. Chambin O, Jannin V. Interest of multifunctional lipid excipients: case of Gelucire 44/14. *Drug DevInd Pharm*. 2005;31:527-534.
14. Huet de Barochez B, Lapeyer F, Cuine A. Oral sustained release dosage forms. Comparison between matrices and reservoir devices. *Drug DevInd Pharm*. 1989;15:1001-1020.
15. Vila-Jato JL, Delgado B. Possible use of Gelucire in controlled nifedipine tablets. *STP Pharma*. 1990;6:88-92.
16. Serajuddin ATM, Sheen PC, Mufson D, Bernstein DF, Augustine MA. Effect of amphiphilicity on the dissolution and bioavailability of a poorly water soluble drug from solid dispersions. *J Pharm Sci*. 1988;77:414-417.
17. Smith A, Lampard JF, Carruthers KM, Regan P. The filing of molten ibuprofen into hard gelatin capsules. *Int J Pharm*. 1990;59:115-119.
18. Chauhan B, Shimpi S, Paradkar A. Preparation and evaluation of glibenclamide-polyglycolized glycerides solid dispersions with silicon dioxide by spray drying technique. *Eur J Pharm Sci*. 2005;26:219-230.
19. Chauhan B, Shimpi S, Paradkar A. Preparation and characterization of etoricoxib solid dispersions using lipid carriers by spray drying technique. *AAPS Pharm. Sci. Tech*. 2005;6:05-12
20. Porter CJ, Charman WN. In vitro assessment of oral lipid based formulations. *Adv. Drug Del. Rev*. 2001;50:127-147.
21. Patil PR, Biradar SV, Paradkar AR. Extended release felodipine self-nano emulsifying system. *AAPS Pharm Sci Tech*. 2009;10:515-523.
22. Ash, Michael, Irene Ash, eds. Handbook of fillers, extenders, and diluents. Synapse Info. Resources. 2007.



23. Gattefosse, Product Literature, Gattefosse (1999). Pharmaceutical excipient for oral semi-solid formulations, Gelucire 44/14-Prompt release and enhanced bioavailability, PF96327, 1st Edition.
24. Sachs-Barrable K, Thamboo A, Lee SD, Wasan KM. Lipid excipients Peceol and Gelucire 44/14 decrease P-glycoprotein mediated efflux of rhodamine 123 partially due to modifying P-glycoprotein protein expression within Caco-2 cells. *J Pharm PharmSci* 2007;10:319-331.
25. Potluri RHK, Bandari S, Jukanti R, Veerareddy PR. Solubility enhancement and physicochemical characterization of carvedilol solid dispersion with Gelucire 50/13. *Arch Pharm Res.* 2011;34:51-57.
26. Kale AA, Patravale VB. Design and evaluation of self-emulsifying drug delivery systems (SEDDS) of nimodipine. *AAPS Pharm Sci Tech.* 2008;9:191-196.
27. Chauhan B, Shimpi S, Mahadik KR, Paradkar A. Preparation and evaluation of floating risedronate sodium-Gelucire® 43/01 formulations. *Drug DevInd Pharm.* 2005;31:851-886.
28. Ortigosa C, Gaudy D, Jacob M, Puech A. The role of Gelucire in the availability of theophylline in semi-solid matrix capsules. A study of factors: pH, melting point, HLB and paddle rotation speed. *Pharm. Acta.Helv.* 1991;66:311-315.
29. Remuñán C, Bretal MJ, Nunez A, Vila Jato JL. Accelerated stability study of sustained-release nifedipine tablets prepared with Gelucire. *Int J Pharm*1992;80:151-159.
30. Baykara T, Yuksel N. The preparation of prolonged action formulations in the form of semi- solid matrix into hard gelatin capsules of oxprenolol I. Thermocap method. *Drug Dev. Ind. Pharm.* 1991;17:1215-1227.
31. Doelker C, Doelker E, Buri P, Waginaire L. The incorporation and *in vitro* release profiles of deliquescent or unstable drug with fusible excipients in hard gelatin capsules. *Drug DevInd Pharm.* 1986;12:1553-1565.
32. Saraiya D, Bolton S. The use of Precirol to prepare sustained release tablets of theophylline and quinidine gluconate. *Drug DevInd Pharm.* 1990;16:1963-1969.
33. Passerini N, Albertini B, Perissuti B. Evaluation of melt granulation and ultrasonic spray congealing as techniques to enhance the dissolution of praziquantel. *Int J Pharm.*2006;318:92-102.
34. Damian F, Blaton N, Naesens, L, Balzarini J, Kinget R, Augustijns P. Physicochemical characterization of solid dispersions of the antiviral agent UC-781 with polyethylene glycol 6000 and Gelucire 44/14. *Eur J Pharm Sci*2000;10:311-22.
35. Damian F, Blaton N, Kinget R, Van den MG. Physical stability of solid dispersions of the antiviral agent UC-781 with PEG 6000, Gelucire 44/14 and PVP K30. *Int J Pharm.* 2002;244:87-98.
36. Khoo KC, Gibaldi M, Brazzell RK. Comparison of statistical moment parameters to  $C_{max}$  and  $T_{max}$  for detecting differences in an in-vitro dissolution rates. *J Pharm Sci.* 1985;74:1340-1342.
37. Bruce JA, Nhung HN, Nancy JR, Susan MR, Munir AH, Susan JW. Amphiphilic vehicles improve the oral bioavailability of a poorly soluble HIV protease inhibitor at high doses. *Int J Pharm.*1997;156:79-88.
38. Sutananta W, Crig DQ, Newton JM. An evaluation of the mechanism of drug release from glyceride bases. *Int J Pharm.*1995;47:182-187.
39. Green JT, Evans BK, Rhodes J, Thomas GA, Ranshaw C, Feyerabend C. An oral formulation of nicotinic for release and absorption in the colon: its development and pharmacokinetics. *Braz J Clin Pharmacol.*1999;48:485-493.
40. MagronP, Rollet M, Taverdet JL, Vergnaud JM. Spherical oral polymer drug device with two polymers for constant drug delivery. *Int J Pharm.* 1987;38:91-97.
41. Bodmeier R, Paeratakul O, Chen H, Zhang W. Formulation of sustained release wax matrices within hard gelatin capsules in a fluidized bed. *Drug DevInd Pharm.* 1990;16:1505-1519.
42. de los Santos CJJ, Pérez-Martínez JI, Gómez-Pantoja ME, Moyano JR. Enhancement of albendazole dissolution properties using solid dispersions with Gelucire 50/13 and PEG 15000. *J Drug DelivSci Technol.*2017;30:1-12.
43. Eedara BB, Bandari S. Lipid-based dispersions of exemestane for improved dissolution rate and intestinal permeability: in vitro and ex vivo characterization. *Artif Cells NanomedBiotechnol.* 2016;45:917-927.
44. Pestieau A, Krier F, LebrunP, Brouwers A, Streeb B, Evrard B. Optimization of a PGSS (particles from gas saturated solutions) process for a fenofibrate lipid-based solid dispersion formulation. *Int J Pharm.* 2015;485:295-305.
45. ChellaN, Tadikonda R. Melt dispersion granules: formulation and evaluation to improve oral delivery of poorly soluble drugs—a case study with valsartan. *Drug DevInd Pharm.* 2015;41:888-897.

46. Eedara, B.B., Veerareddy, P.R., Jukanti, R.,Bandari, S., 2013. Improved oral bioavailability of fexofenadine hydrochloride using lipid surfactants: ex vivo, in situ and in vivo studies. *Drug Dev. Ind. Phar.* 40,1030-1043.
47. Faisal W, Ruane-O'Hora T, O'Driscoll CM, Griffin BT. A novel lipid-based solid dispersion for enhancing oral bioavailability of Lycopene–In vivo evaluation using a pig model. *Int J Pharm.* 2013;453:307-314.
48. Falconer JR, Wen J, Zargar-Shoshtari S, Chen JJ, Farid M, El Maghraby GM,Alany RG. Evaluation of progesterone permeability from supercritical fluid processed dispersion systems. *Pharm Dev Technol.* 2014;19:238-246.
49. Kim MS, Kim JS, Cho W, Cha KH, Park HJ, Park J, Hwang SJ. Supersaturatable formulations for the enhanced oral absorption of sirolimus. *Int J Pharm.* 2013;445:08-116.
50. Upadhyay P,Pandit JK. Formulation of fast-release gastroretentive solid dispersion of glibenclamide with gelucire 50/13. *Trop J Pharma Res.* 2012;11:361-369.
51. M Shaikh S, M Avachat A. Enhancement of solubility and permeability of candesartan cilexetil by using different pharmaceutical interventions. *Curr Drug Del.* 2011;8:346-353.
52. Bikiaris D, Karavelidis V,Karavas E. Effectiveness of various drug carriers in controlled release formulations of raloxifeneHCl prepared by melt mixing. *Curr Drug Del.* 2009;6:425-436.
53. Babu AK, Ramana MV. Development and *in vivo* evaluation of gastroretentive floating tablets of antipsychotic drug Risperidone. *Int J Pharm Pharm Sci.* 2016;8:43-52.
54. Arza RAK, Kumar BV. Development and evaluation of gastroretentive floating matrix tablets of moxifloxacin HCL. *PharmLett.* 2016;8:140-149.
55. Jammula S, Patra CN, Swain S, Panigrahi KC, Nayak S, Dinda SC, Rao MEB. Design and characterization of cefuroxime axetil biphasic floating minitables. *Drug Deliv.* 2015;22:125-135.
56. Juárezsoberanez D, Villa fuerterobles L. Gelucire 39/01 as excipient for gastroretentive metronidazole sustained delivery. *Int JPharm Sci.* 2011;3:86-91.
57. Patel DM, Patel MJ, Patel AN, Patel CN. Formulation and evaluation of mixed matrix gastro-retentive drug delivery for famotidine. *Int J PharmInvestig.* 2011;1:247-252.
58. Ramesh KVRNS,Ravishankar P, Indira V, Kumar AP. Hydrophilic and Hydrophobic Gelucires in the Design and Evaluation of Controlled Release Matrix Tablets of Nifedipine. *Int J Chem Sci.* 2011;9-13.
59. Bhikshapathi D, Kumar JA, Suresh G, Viswaja M, Ramesh B. Gastroretentive floating capsules of Risedronate Sodium: Development, optimization, in vitro and in vivo evaluation in healthy human volunteers. *Int J Pharm Sci Nano.* 2015;8:2835-2842.
60. Kalpana M, SistlaR,Shastri NR. Modulating drug release profiles by lipid semi solid matrix formulations for BCS class II drug–an in vitro and an in vivo study. *Drug Deliv.* 2015;22:418-426.
61. Bhalekar M, Upadhaya P,Madgulkar A. Formulation and characterization of solid lipid nanoparticles for an anti-retroviral drug darunavir. *ApplNanosci.* 2017;7:47-57.
62. Garg NK, Singh B, Tyagi RK, Sharma G,Katara OP. Effective transdermal delivery of methotrexate through nanostructured lipid carriers in an experimentally induced arthritis model. *Colloids Surf BBiointerfaces.* 2016;147:17-24.
63. Ochiuz L, Grigoras C, Popa M, Stoleriu I, Munteanu C, Timofte D, Profire L, Grigoras AG. Alendronate-Loaded Modified Drug Delivery Lipid Particles Intended for Improved Oral and Topical Administration. *Molecules.* 2016;21:858-873.
64. Khan A, Imam SS, Aqil M, Ahad A, Sultana Y, Ali A, Khan K. Brain Targeting of Temozolomide via the Intranasal Route Using Lipid-Based Nanoparticles: Brain Pharmacokinetic and Scintigraphic Analyses. *Mol Pharm.* 2016;13:3773-3782.
65. Hazzah HA, Farid RM, Nasra M, Hazzah WA, El-Massik MA,Abdallah OY. Gelucire-Based Nanoparticles for Curcumin Targeting to Oral Mucosa: Preparation, Characterization, and Antimicrobial Activity Assessment. *J Pharm Sci.* 2015;104:3913-3924.
66. Oyewumi MO, Wehrung D,Sadana P. Gelucire-stabilized nanoparticles as a potential DNA delivery system. *PharmDev Technol.* 2015;21:647-654.
67. Gonsalves VSS, Matias AA, Rodríguez-Rojo S, Nogueira ID, Duarte CMM. Supercritical fluid precipitation of ketoprofen in novel structured lipid carriers for enhanced mucosal delivery–a comparison with solid lipid particles. *Int J Pharm.* 2015;495:302-311.

68. Čerpnjak K, Zvonar A, Vrečer F, Gašperlin M. Characterization of naproxen-loaded solid SMEDDSs prepared by spray drying: The effect of the polysaccharide carrier and naproxen concentration. *Int J Pharm.* 2015;485:215-228.
69. Wehrung D, BiL, Geldenhuys WJ, Oyewumi MO. Antitumor efficacy and tolerability of systemically administered gallium acetylacetonate-loaded Gelucire-stabilized nanoparticles. *J Biomed Nanotechnol.* 2013; 9:1029-1040.
70. Wehrung D, Geldenhuys WJ, BiL, Oyewumi MO. Biocompatibility, efficacy and biodistribution of gelucire-stabilized nanoparticles engineered for docetaxel delivery. *J Nanosci Nanotechnol.* 2012;12:2901-2911.
71. Date AA, Vador N, Jagtap A, Nagarsenker MS. Lipid nanocarriers (GeluPearl) containing amphiphilic lipid Gelucire 50/13 as a novel stabilizer: fabrication, characterization and evaluation for oral drug delivery. *Nanotechnol.* 2011;22:1-12.
72. Albertini B, Sabatino MD, Melegari C, Passerini N. Formulation of spray congealed microparticles with self-emulsifying ability for enhanced glibenclamide dissolution performance. *J Microencapsul.* 2015;32:181-192.
73. Breitzkreitz MC, Sabin GP, Polla G, Poppi RJ. Characterization of semi-solid Self-Emulsifying Drug Delivery Systems (SEDDS) of atorvastatin calcium by Raman image spectroscopy and chemometrics. *J Pharm Biomed Anal.* 2013;73:3-12.
74. Kanaujia P, Ng WK, Tan RB, 2014. Solid self-emulsifying drug delivery system (S-SEDDS) for improved dissolution rate of fenofibrate. *J Microencapsul.* 2014;31:293-298.
75. Siripuram PK, Bandari S, Jukanti R, Veerareddy PR. Formulation and characterization of floating gelucire matrices of metoprolol succinate. *Dissolut Technol.* 2010;17:34-39.
76. Chauhan B, Shimpi S, Mahadik KR, Paradkar A. Preparation and evaluation of floating risedronate sodium Gelucire® 39/01 matrices. *Acta Pharmaceutica.* 2004;54:205-214.
77. Soni S, Verma N, Verma A, Pandit JK. Gelucire based floating emulsion gel beads: a potential carrier for sustained stomach specific drug delivery. *Farmacia.* 2017;65:142-152.
78. Ammar HO, Ghorab MM, Mahmoud AA, Noshi SH. Formulation of risperidone in floating microparticles to alleviate its extrapyramidal side effects. *Future J Pharm Sci.* 2016;2:43-59.
79. Kumar S, Mishra AK. Preparation and evaluation studies on sustained release of furosemide using lipid excipient. *Pharm Lett.* 2016;8:243-250.
80. Tiwari P, Soni S, Ram V, Verma A. Raft forming buoyant pH dependent thixotropic gelling systems incorporated with gelucire 43/01 as a potential stomach specific drug delivery system for famotidine. *J Appl Pharm.* 2015;7:183-202.
81. Upadhyay P, Pandit JK, Wahi AK. Studies on biological macromolecules lipid-Gelucire based gastroretentive multiparticulate. *Int J Biol Macromol.* 2014;67:463-477.
82. Saxena A, Mishra AK, Verma N, Bhattacharya SS, Ghosh A, Verma A, Pandit JK. Gelucire based in situ gelling emulsions: a potential carrier for sustained stomach specific delivery of gastric irritant drugs. *Biomed Res Int.* 2013;1-11.
83. Adel S, ElKasabgy NA. Design of innovated lipid-based floating beads loaded with an antispasmodic drug: in-vitro and in-vivo evaluation. *J Liposome Res.* 2014;24:136-149.
84. Pawar YB, Purohit H, Valicherla GR, Munjal B, Lale SV, Patel SP, Bansal AK. Novel lipid based oral formulation of curcumin: Development and optimization by design of experiments approach. *Int J Pharm.* 2012;436:617-623.
85. Rao MEB, Swain SS, Patra CN, Sruti J, Patra S. Development and in vitro evaluation of floating multiparticulate system of repaglinide. *FABAD J Pharm Sci.* 2011;36:75-92.
86. Shimpi S, Chauhan B, Mahadik KR, Paradkar A. Preparation and evaluation of diltiazem hydrochloride-Gelucire 43/01 floating granules prepared by melt granulation. *AAPS Pharm Sci Tech.* 2004;5:51-56.