Investigation of structural and phase transition of high purity monoglyceride-water systems

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Abstract

Effective drug delivery requires the **precise spatial** and **temporal delivery** of therapeutic agents to the target site. Triggerable drug delivery systems have the ability to effectively switch drug release on or off from a depot at will providing great control over the potential effectiveness and safety of the therapy.

The hypothesis of this project is that an appropriate blend of monoglycerides will provide a biocompatible and physiological, nontoxic, thermo-responsive matrix that melts at 42°C initiating drug release and solidifies at 37 °C to slow down or terminate the release (Fig 1).

Introduction

The phase behavior of amphiphilic lipids and surfactants at various relative humidity levels and water content is of great interest for many technical and pharmaceutical applications.

Monoglycerides, such as glyceryl monolaurate (GML), glyceryl monooleate (GMO) and glyceryl monostearate (GMS) are self-assembling amphiphilic molecules that form a variety of crystalline structures with useful mechanical properties of special interest in drug delivery. Recently we evaluated lipid matrices containing mixtures of monoglycerides for their potential application as magnetically induced thermo-responsive local drug delivery systems (Fig. 1).

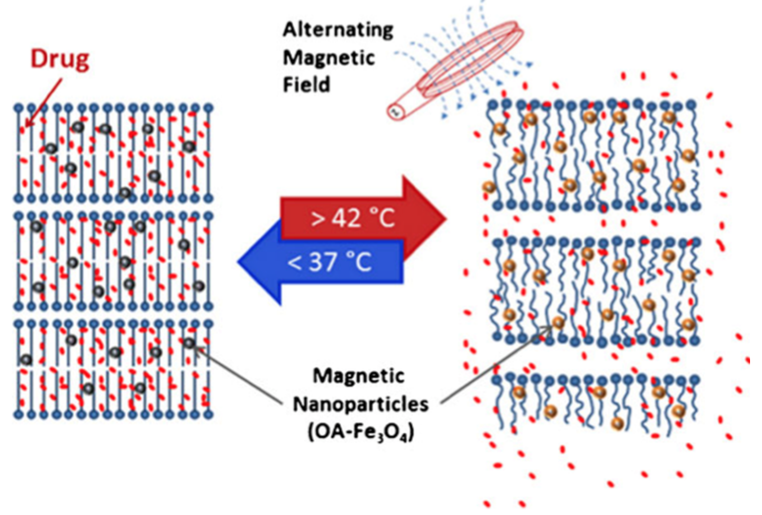


Fig 1. Triggerable lipid matrix that melts and releases drug at 42° C and solidifies to stop drug release at 37° C

However, the presence of excess moisture or hydrophilic additives such as ethanol, PG, and PEG 400 are reported to influence the phase behavior of monoglycerides and induce conversion of the crystalline arrangement into a low melting point polymorph that releases the drug faster.

Objectives

1. Investigate how moisture affects the crystalline structure of the monoglyceride matrix
2. Determine at what percentage of moisture (if any) will the monoglyceride matrix fail to serve as a thermo-responsive excipient.

Methods

Investigation of the effect of moisture on monoglycerides structure

- Monoglycerides were stored at various relative humidities for a period of 1 week
- The gain or loss of weight, as well as the melting points, relaxation temperature and heat of fusion were determined using differential scanning calorimetry (DSC)

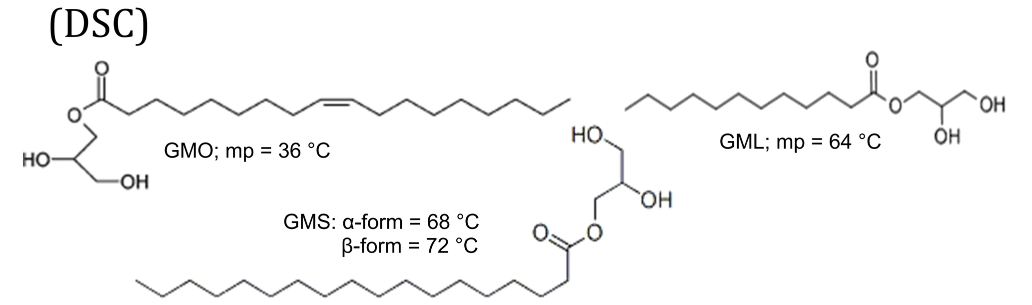


Fig 2. Chemical structures of the lipids

Determination of the phase behavior of the monoglyceride matrices

- Prepare 0 – 100 w/w% GMO:GMS mixtures
- Determine the crystallization behavior of the matrices using DSC

Direct addition of water

- Deionized water was added to GML in DSC aluminum pans at different percentages: 58%, 26%, 18%, 10%, 12.7%, and 7% and analyzed using DSC

Results

Melting points of GMO:GMS Mixtures

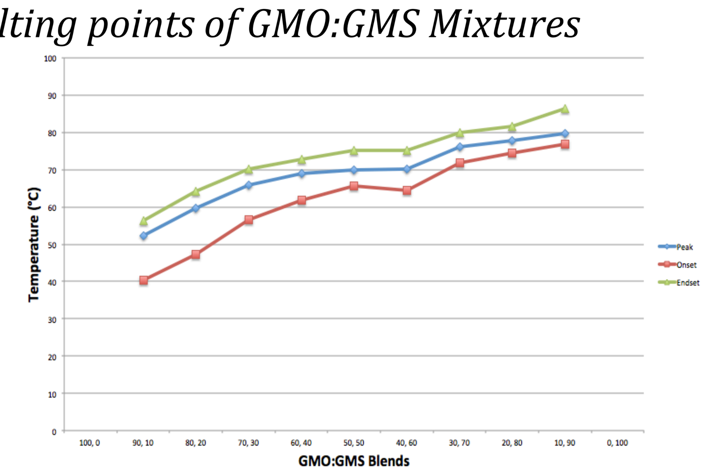
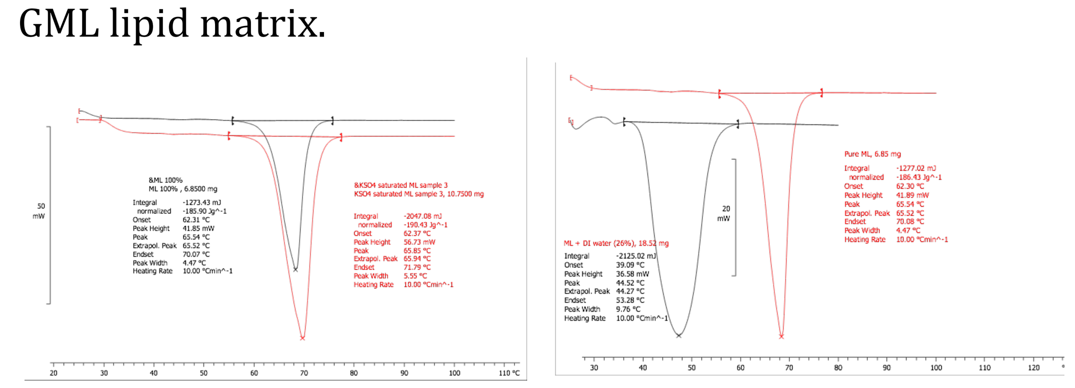


Fig 3. Melting points of GMO:GMS blends

Effect of moisture on crystalline structure of pure monoglycerides

Our results show that increased relative humidity, of 75% and 97%, does not significantly affect the structure of the GML lipid matrix.



GML stored at 75% RH *GML with 26% water*

Fig 4. Effect of moisture on crystalline structure of pure monoglycerides

Percent moisture uptake/loss of 50:50 w/w% GMO:GMS matrix at 25 °C

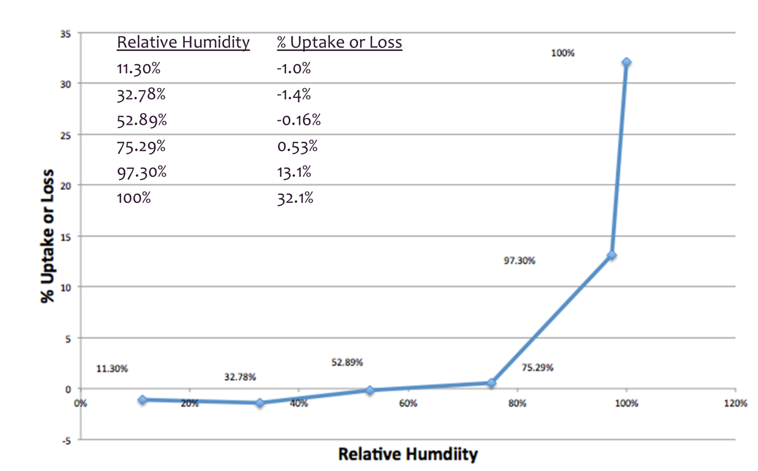


Fig 5. GMO:GMS (50:50) moisture uptake/loss

DSC of GMO:GMS (50:50) samples after stored at different relative humidity

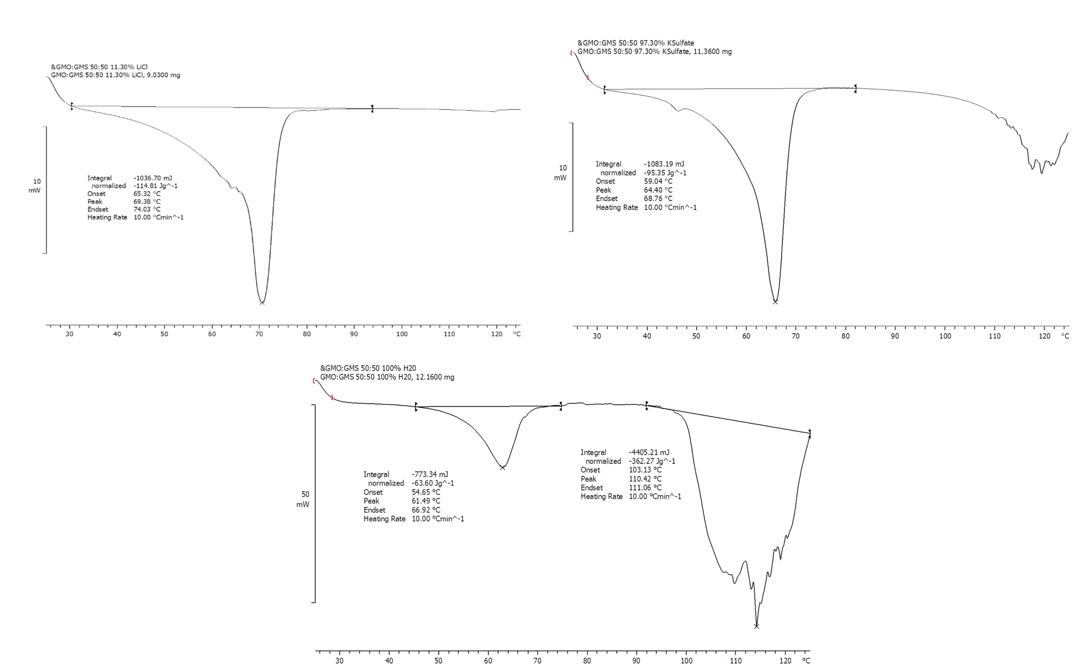


Fig 6. DSC of GMO:GMS matrices

Table 1: Specific heat of fusion (enthalpy) of 50:50 w/w% GMO:GMS matrices at 11, 97 and 100% relative humidity (RH)

RH	Moisture uptake	peak T*m*	Normalized heat of fusion	Heat of fusion (weight of GMO:GMS)
11%	-1.0%	69.4 °C	114.8 J/g	113.7 J/g
97%	13.1%	64.4 °C	95.35 J/g	109.6 J/g
100%	32.1%	61.5 °C	63.60 J/g	93.7 J/g

SEM of GMO:GMS (50:50) stored at various relative humidity levels

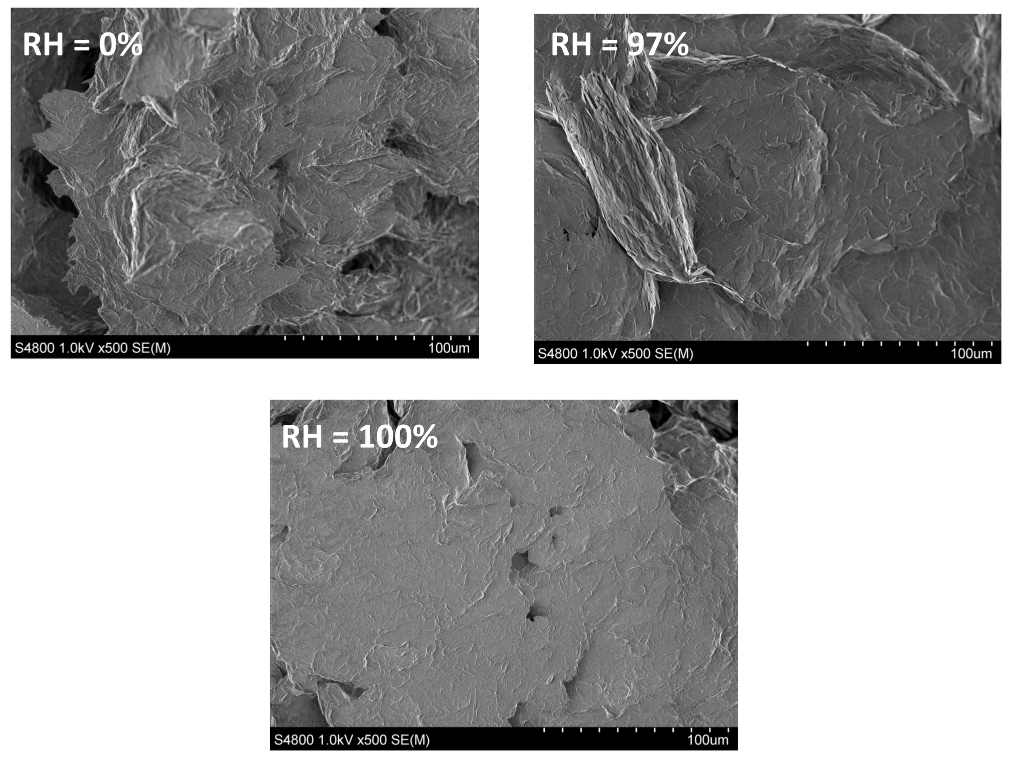


Fig 7. SEM of GMO:GMS matrices

Conclusion

These findings tell us that the crystalline structure of the monoglyceride blend was maintained and was not significantly affected by increased levels of moisture, indicating their potential as a thermo-responsive excipient in the smart drug delivery system.

Acknowledgements

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