Miconazole nanoemulsions for melanoma treatment:

formulation development and droplet size and solubility studies

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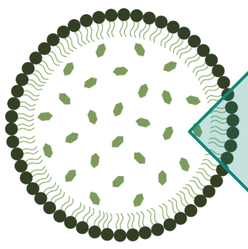
Background

- **Melanoma** is one of the most dangerous skin cancers, with a high mortality rate and an incidence that has increased radically in the past few years. This has led to a huge demand for new more effective forms of treatment [7,8,11].
- Miconazole has shown to **inhibit the growth of melanoma cells**[2,5].

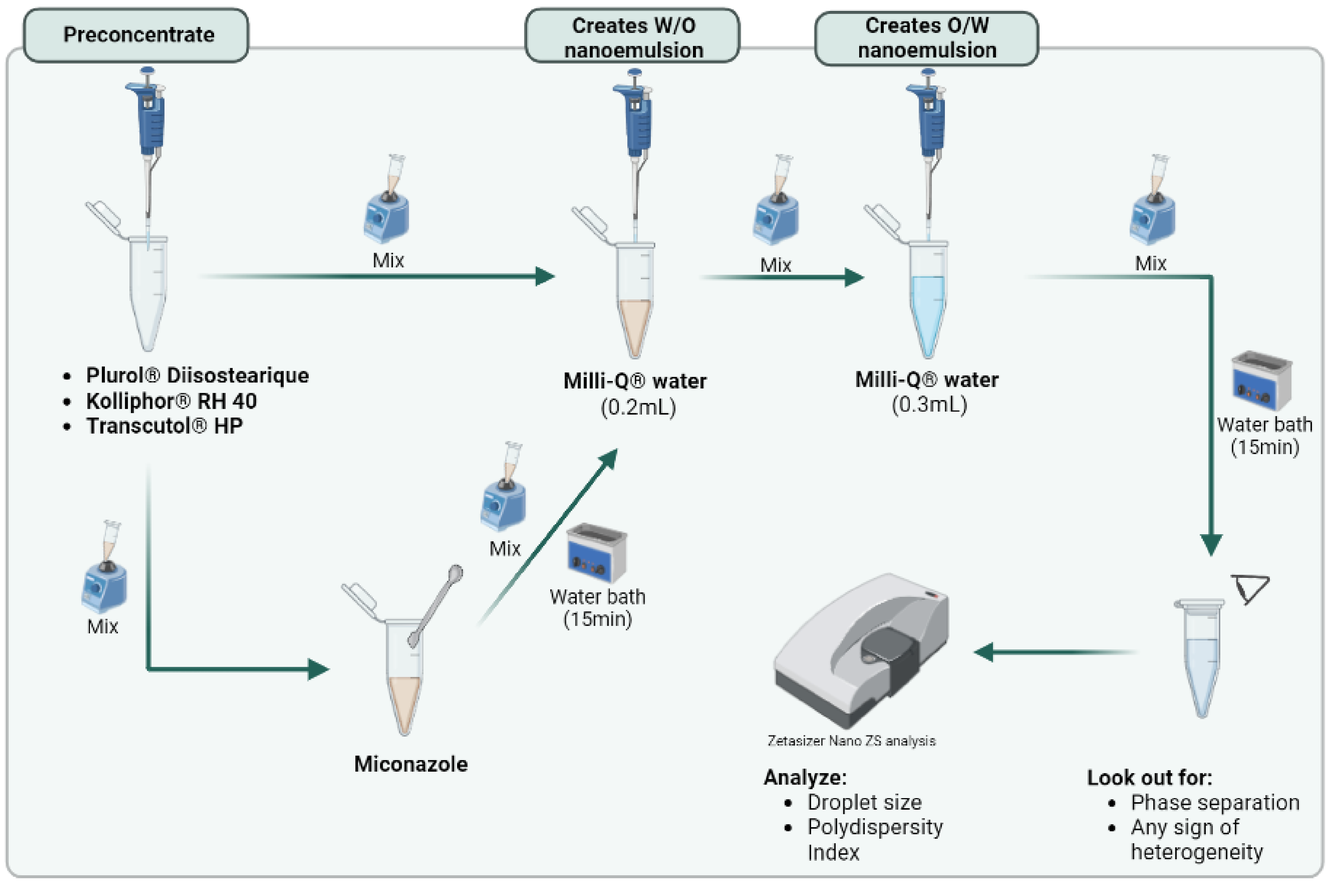


Nanoemulsions have been investigated as potential drug delivery vehicles to target cancer cells, since they are a promising alternative to increase the solubility and skin permeation and retention of hydrophobic drugs.[3,4,7,9]

Purpose

The purpose of this work was to incorporate **miconazole**, a hydrophobic[12] antifungal drug with **potential anticancer activity**[2,5], in an oil-in-water (O/W) nanoemulsion for topical administration for the treatment of melanoma.

Methodology



Results

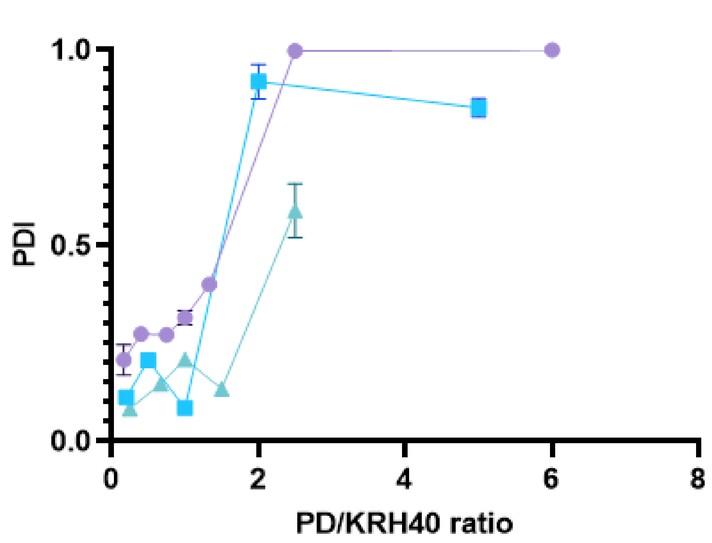
- After phase 1 (nanoemulsion without miconazole), **2 out of the 17 nanoemulsions** had promising characteristics– PDI below 0.300 and droplet size between 100 and 200 nm.

Nanoemulsions with higher %Transcutol® HP had a lower PDI

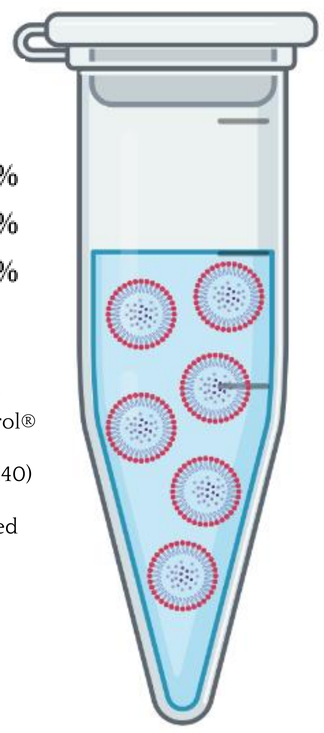
- This is expected, since this excipient is used as a co-emulsifier. It is used to achieve a ultralow interfacial tension, and helps make the emulsion more fluid [1,6].

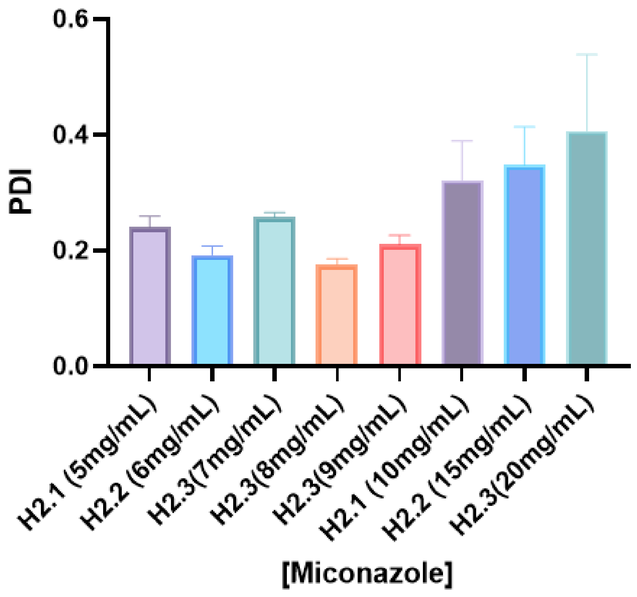
Nanoemulsions with high quantities of Kolliphor® RH 40 had a lower PDI

- This is expected, since Kolliphor can reduce nanoemulsion droplet size, probably because of its chemical structure with a lot of polyethylene glycol groups and therefore higher hydrophilic. This is also expressed by the higher hydrophilic-lipophilic balance (HLB) value of Kolliphor (HLB = 14– 16).[10]

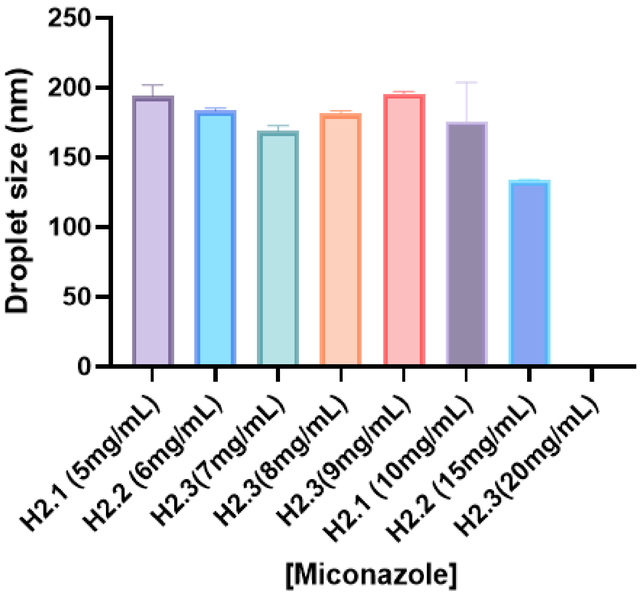


Graphic 1. Relationship between polydispersity index (PDI) and the Plurol® Diisostearique (PD)/ Kolliphor® RH 40 (KRH40) ratio in the seventeen nanoemulsions prepared in phase 1.





Graphic 2. Mean polydispersity index of nanoemulsions with different miconazole concentrations (mg/mL).



Graphic 3. Mean droplet size of nanoemulsions with different miconazole concentrations (mg/mL).

We consider the formulations to maintain good characteristics if miconazole is solubilized and the nanoemulsion keeps:

PDI < 0.300
Droplet size between 100 and 200 nm

Considering the above information, just 1 of the 2 nanoemulsions (from phase 1) had good characteristics.

Solubility assays proved it was possible to have:

5-9 mg/mL [Miconazole] → Drug strength 11 795 times higher than the drug's water solubility

Conclusion

- It is possible to **develop nanoemulsions** with good characteristics and **high miconazole concentration**. It allows to greatly **increase** miconazole **solubility** when compared to water (up to 11 795 times).
- **This formulations could be useful for the treatment of melanoma**, as this drug has been shown to decrease the growth of this type of cancer cells at much lower concentrations.
- Future studies will include determination of viscosity, stability, *in vitro* drug release, *ex vivo* drug permeation and *in vitro* cytotoxicity in melanoma cells.

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