Sneak Peek

Lipid Based Formulations

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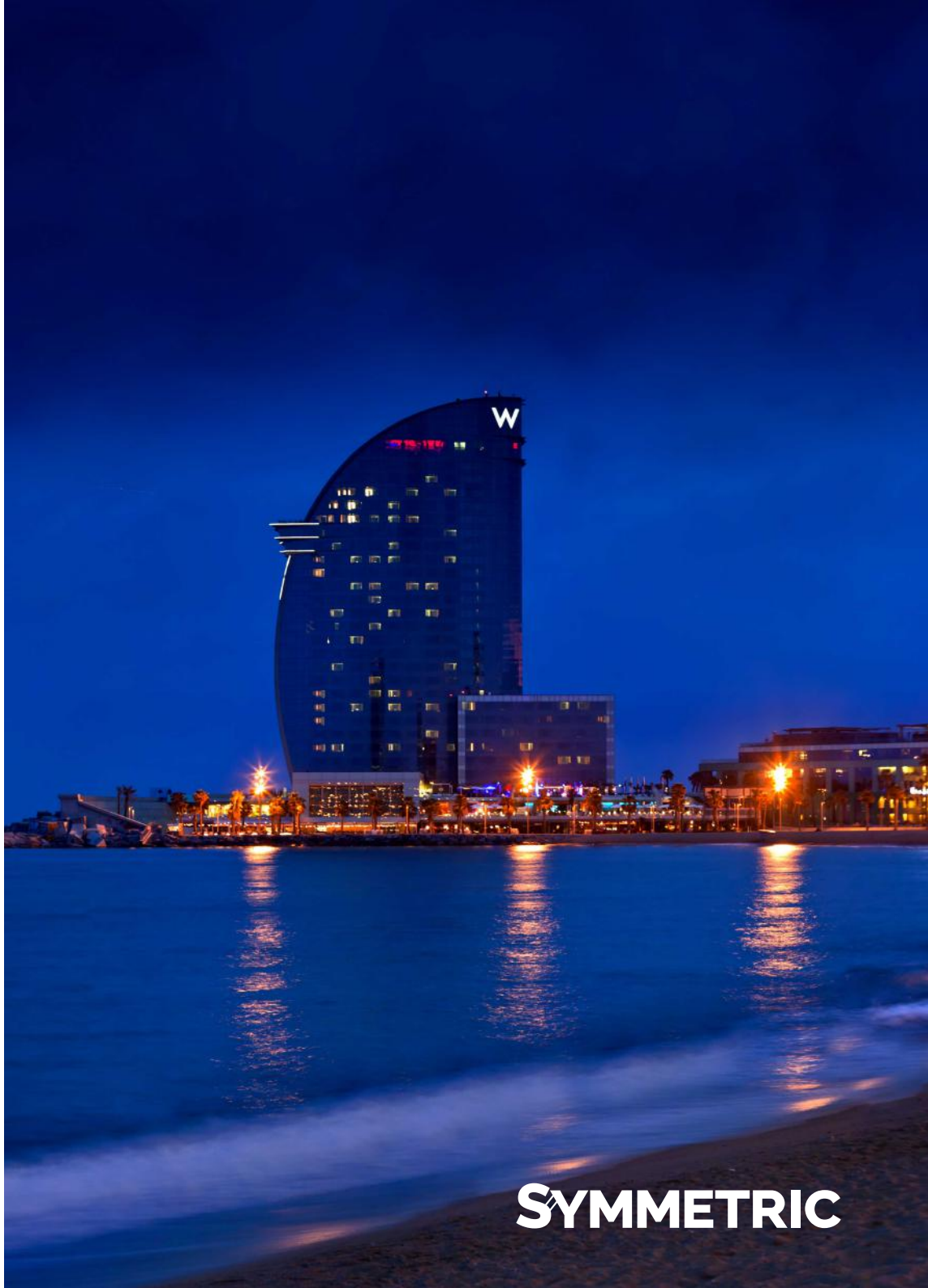
ONLINE
TRAINING



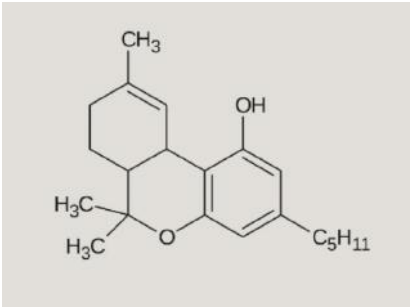
Introduction to the World of Lipids

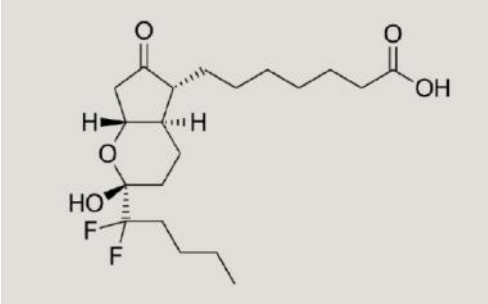
01

What they do, and how pharmaceutical development can benefit

Alone, or in combination, lipid based excipients can be used to present lipophilic drugs in solution. It sounds too good to be true, but there are commercial examples of this type of formulation!

Dronabinol or delta-9-tetrahydrocannabinol, the active ingredient is Marinol®, is **extremely lipophilic (log P>5) and simply solubilised in Sesame Oil**





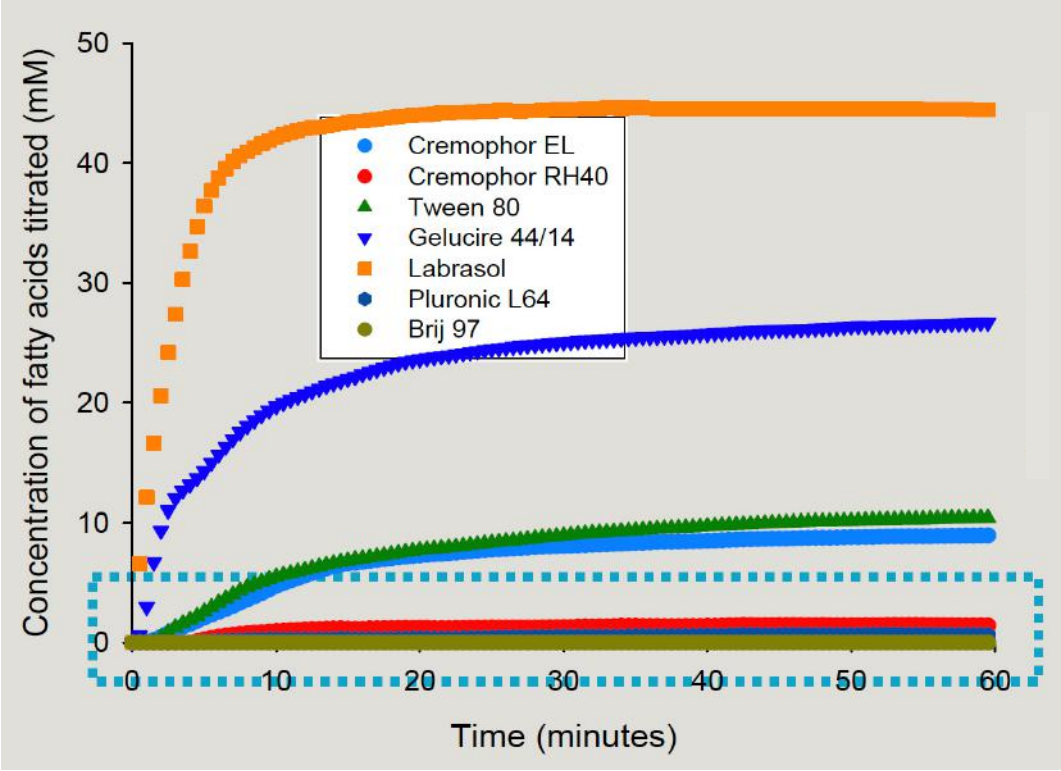
Lubiprostone, the active ingredient in Amitiza®, **is in solution in MCT**, even if the drug is not absorbed (local action against IBS), a solution that facilitated analytics for 8 mcg dose

Source: Dr. Eduardo Jule, Evolve Consulting

Harnessing the Power of Physiological Pathways

Solubilisation and Oral Bioavailability enhancement of small molecules

So then, individual surfactants —and not only oils— are digested, giving the story a whole new twist!



- *Labrasol, a blend primarily composed of C8/C10 glycerides coupled to PEG 400 (but also mono-, di- and even triglycerides) is, understandably, heavily digested*
- *Gelucire, a similar structure containing PEG 1500/ coconut oil esters is 2nd given a **relatively larger outer corona** that hinders lipase access to the O/W interface*
- *Pluronic L64 (poloxamer 186, a tri-block copolymer PEG-PPG-PEG) and Brij 97 (PEG10-oleyl ether) are immune to the process, providing further control to the experiment*

Source: Dr. Eduardo Jule, Evolve Consulting

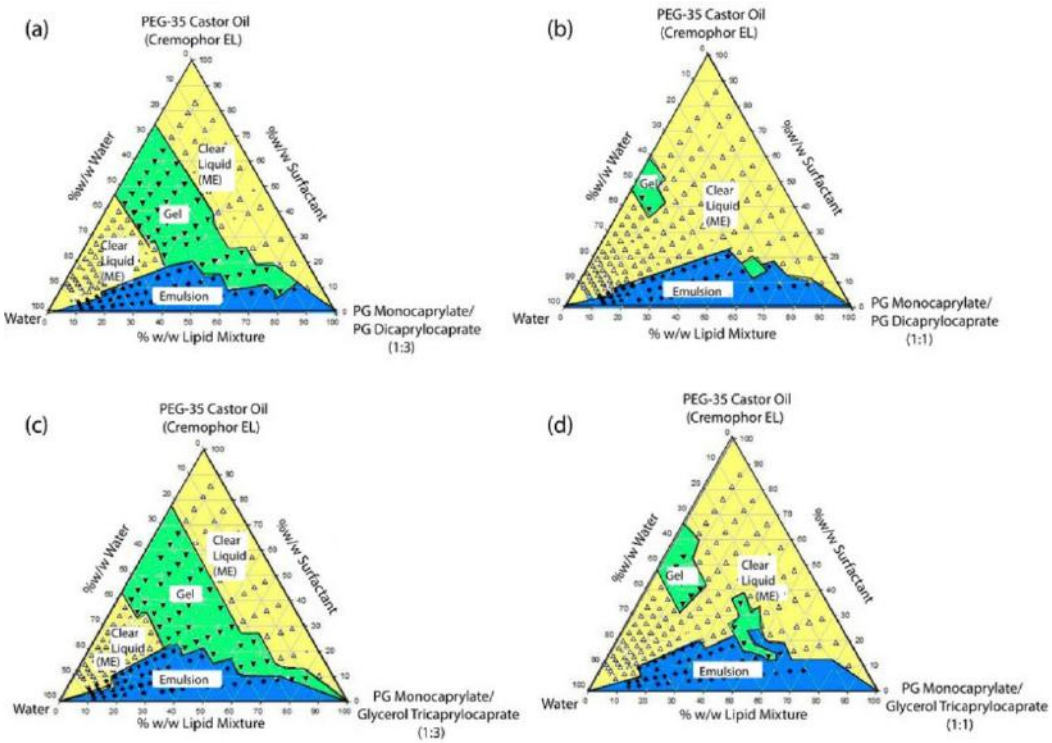
Understanding and Predicting Performance

The Lipid Formulation Classification System

And this is where most people freak out.

- *SEDDS are **delivered as pre/concentrates**, ie emulsions or microemulsions minus the water*
- *Which means their **behaviour on dispersion needs to be characterised and understood***
- *Generally, a lipophilic (eg oils/low HLB cosurfactants are opposed to a hydrophilic (eg high HLB surfactant/co-surfactant/co-solvent, which must then be dispersed with water*
- *Ideally, the system consistently forms an emulsion or microemulsion (remember, droplet particle size is not your critical parameter!) regardless of the amount of water in the environment*

Patel et al., J. Excipients and Food Chemicals 2012, 3 (2)



Source: Dr. Eduardo Jule, Evolve Consulting

Keys to Successful Formulation Design and Development

04

Developing an unbiased view on technology selection

The overwhelming majority of **new chemical entities** (NCEs) emerging out of drug discovery **display low solubility, which leads to poor and/or erratic oral Bioavailability** (BA). As a consequence, both the need and use of enabling drug delivery technologies has become widespread. As the number of commercial successes grows, a virtuous cycle of acceptance grows

Solid State, Particle Engineering

Polymorphism

Particle Size Reduction

Amorphous Solid Dispersions (ASD)

- Spray dried dispersions (SDD)
- Hot melt extrusions (HME)

Nanocrystals

Top-down micronisation or nano-milling are used to fragment particles by dry-impact processes that utilise high shear forces (from hammer to jet-air mills), generating particles in 0.2-5 µm range. Bottom up nanocrystallisation controls crystallisation or precipitation of drug assemblies. Both are useful for overcoming instances where the dissolution rate is too slow to maintain drug concentration at its equilibrium in the intestine

Pros: *increased surface areas, no enabling technologies though excipients or additives often required*

Cons: *particles are cohesive, need to be stabilised to prevent aggregation, limited coverage, ie even if dissolution rate becomes instant, low levels of thermo solubility limit ability create drug concentration gradient, potential polymorph*

Source: Dr. Eduardo Jule, Evolve Consulting

Registration

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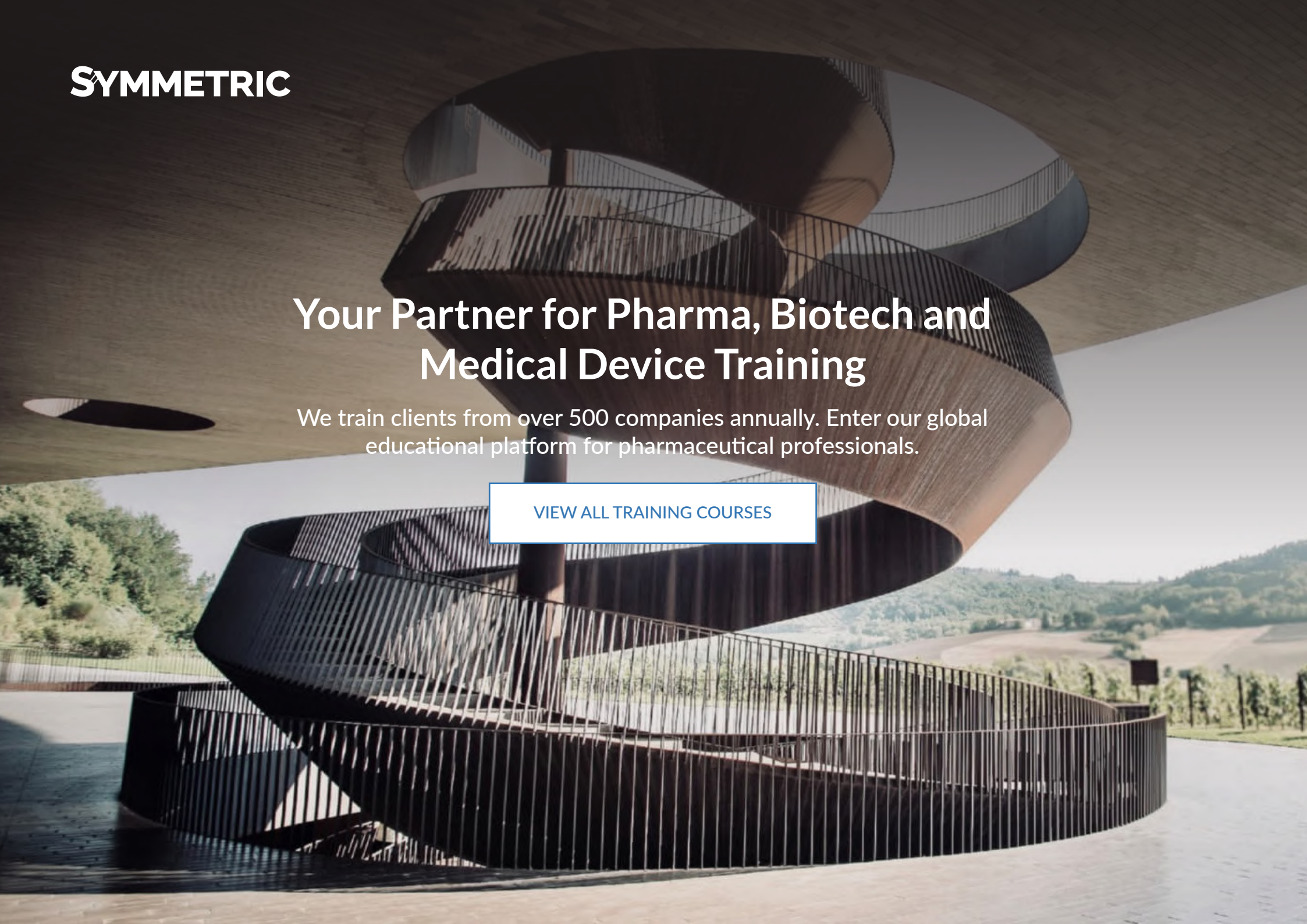
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