

Croda Pharma

# Formulation solutions for cannabinoids (CBD)

September 2022

Smart science to improve lives™

CRODA

# Agenda

- Sustainability
- Our journey to Croda Pharma
- How Croda is meeting the trends
- Solubility guide
- Croda's solutions



# Our commitment for a sustainable future



## 2030 target

We are committed to being the most sustainable supplier of innovative ingredients.

“We take great pride in the extraordinary commitment from our people, who are using Smart science to improve lives™.”

**Steve Foots, Group Chief Executive**



## Reducing Emissions



We will reduce **carbon emissions** aligned to our verified Science Based Target, supporting our customers with their **Net Zero** goals.



## Health & Wellbeing



We will contribute to the successful development and commercialisation of **25% of WHO\* listed pipeline vaccines**.



# Our journey to Croda Pharma

**1925**

Croda was founded



**2000 onwards**

Ongoing investments in high purity excipients



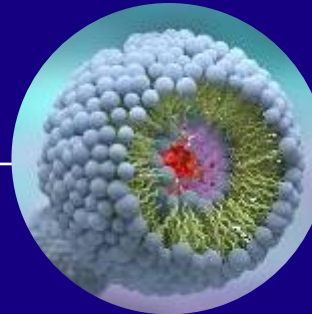
**2019**

Biosector acquisition, industry leading vaccine adjuvants



**2020**

Acquisition of world leading lipid portfolio



**2021**

Global investments in pharma +£100m – a commitment to advancing expertise



**2022**

Our Health Care business becomes



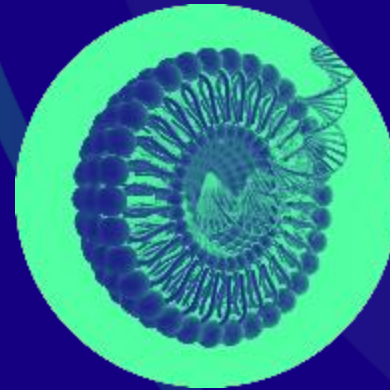
# Croda Pharma platforms



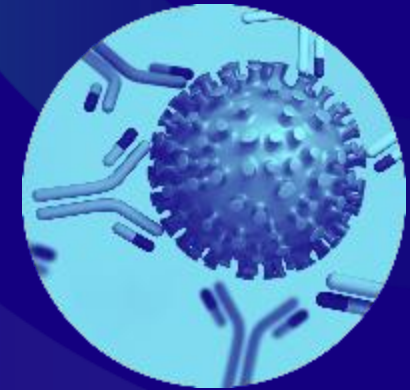
**Small Molecule  
Delivery**



**Protein  
Delivery**



**Nucleic Acid  
Delivery**



**Adjuvant  
Systems**

**Human and Veterinary Health**

# Consumer Health

We combine our **technical expertise** with **regulatory knowledge** to help our customers market innovative products with **consumer relevant claims**, alongside supporting **formulation development challenges** within the Consumer Health market.

Excipient solutions for:

**OTC**  
*(Over-the-Counter)*

**Nutraceutical  
supplements**

Softgels

Patches

Eye  
Care

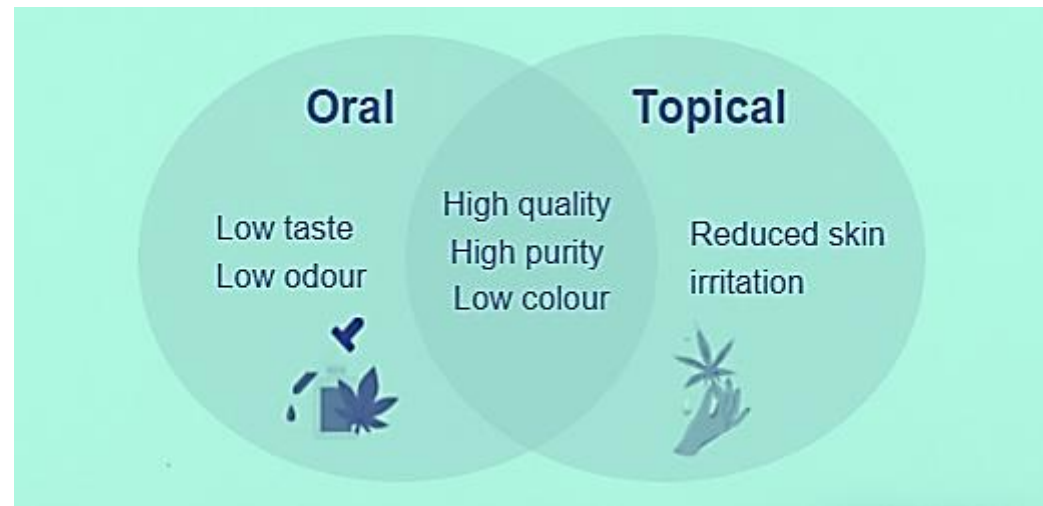
CBD





# How Croda is meeting the trends

The use of cannabidiol (CBD) in health care is clearly a growing trend, check out Croda's Super Refined™ product solutions.



Super Refining is a unique purification process that eliminates impurities, that cause skin irritation and improves organoleptic properties.

# Value of high purity excipients

The meaning of purification	Benefits of excipient	Value to the customer
<p>Removal of problematic impurities</p> <ul style="list-style-type: none"><li>▪ Moisture</li><li>▪ Residual catalysts</li><li>▪ Peroxides</li><li>▪ Aldehydes</li></ul>	<ul style="list-style-type: none"><li>▪ Improved API and formulation stability</li><li>▪ Reduced taste impact</li><li>▪ Analytical clarity</li><li>▪ Multi-compendial</li></ul>	<ul style="list-style-type: none"><li>▪ Faster drug development time</li><li>▪ Increased speed to market</li><li>▪ Improved drug shelf-life</li><li>▪ Lower drug development costs</li></ul>

← Experience the Super Refined™ solution →



# CBD formulation challenges

## Challenge

- Oxidation tendency
- Poor solubility
- Low permeability
- Poor bioavailability

## Croda solution – Super Refined™ technology

- Reduces risk of oxidation stability – shelf life extended
- Lipophilic compound delivery technology
- Effective delivery enhancement mechanism
- A self-emulsifying and self microemulsifying delivery system (SEDDS and SMEDDS)



# CBD solubility guide

Product name	Inactive ingredient	Solubility (mg/g)	USP solubility
Super Refined™ DMI	Dimethyl isosorbide	778.5	very soluble
Super Refined™ DEGEE	Diethylene glycol monoethyl ether	746.3	very soluble
Super Refined™ PEG 400	Polyethylene glycol 400	593.9	very soluble
Super Refined™ CCMG 400	Caprylocaproyl macrogolglycerides	563.7	very soluble
Super Refined™ P35 Castor Oil	Polyoxyl 35 castor oil	522.2	very soluble
Super Refined™ Polysorbate 80	Polysorbate 80	512.3	very soluble
Super Refined™ Crodamol IPM	Isopropyl myristate	510.9	very soluble
Super Refined™ GMCC	Glycerol monocaprylo caprate	459.8	freely soluble
Super Refined™ GTCC	Caprylic/capric triglyceride	465.4	freely soluble
Super Refined™ Corn Oil	Corn oil	287.5	freely soluble
Super Refined™ Sesame Oil	Sesame oil	280.7	freely soluble
Super Refined™ Olive Oil	Olive oil	118.9	freely soluble

# CBD excipients application and monograph

Product name	HLB	Application						Monograph				
		topical	oral	transdermal	ophthalmic	nasal/ auricular	injectable	rectal	PhEur	USP/NF	JP/JPE	FDA IID
**Super Refined™ DMI	-	x			x							
Super Refined™ DEGEE	-	x	x		x				x	x		x
Super Refined™ PEG 400		x	x			x	x	x	x	x	x	x
Super Refined™ CCMG 400	-	x	x		x				x	x		x
Super Refined™ P35 Castor Oil	14*	x	x			x	x		x	x	x	
Super Refined™ Polysorbate 80	15	x	x			x	x	x	x	x	x	x
Super Refined™ IPM	10.0*	x			x			x	x	x	x	x
Super Refined™ GMCC	-	x	x		x				x	x		
Super Refined™ GTCC	10*	x	x		x				x	x	x	x
Super Refined™ Corn Oil	7.9*		x				x		x	x		x
Super Refined™ Sesame Oil	7.8*		x				x		x	x	x	x
Super Refined™ Olive Oil	7.7*	x	x									x

\*Required HLB, \*\*monograph publication pending

Croda's pharmaceutical solubility data can be found here <https://www.crodapharma.com/en-gb/resources/pharmaceutical-solubility-guide>

# Topical / transdermal formulations

## Forms

- Pain relief creams
- Gels
- Ointments
- Transdermal patches

*The skin is an excellent barrier, and that can make it challenging for topical drug delivery.*

## Key products

**Super Refined™ DMI** improves spreading, enhances the delivery of actives

**Super Refined Oleic Acid** improves drug delivery into the skin and reduces skin irritation

**Super Refined DEGEE** enhances the permeation of poorly water-soluble API's

Our formulation experts can help to guide you in the right direction on which penetration enhancer to choose.



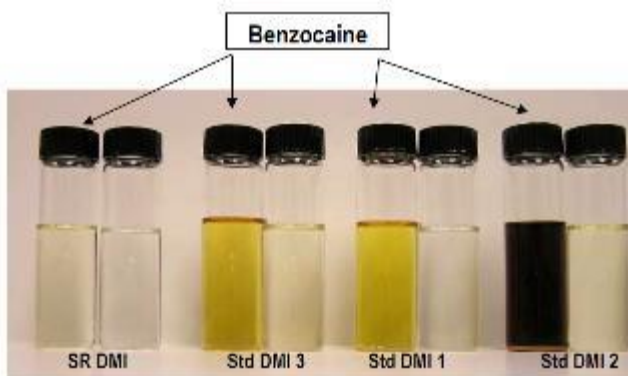
# Super Refined™ DMI

## HIGHLY PURIFIED DIMETHYL ISOSORBIDE

### Features

- Solvent for poorly soluble hydrophilic and hydrophobic actives
- Enhances formulation and API stability
- Epidermal penetration enhancer
- Improves spreading of viscous materials
- Reduced cellular irritation
- Reduced API oxidation rate

### Penetration enhancing

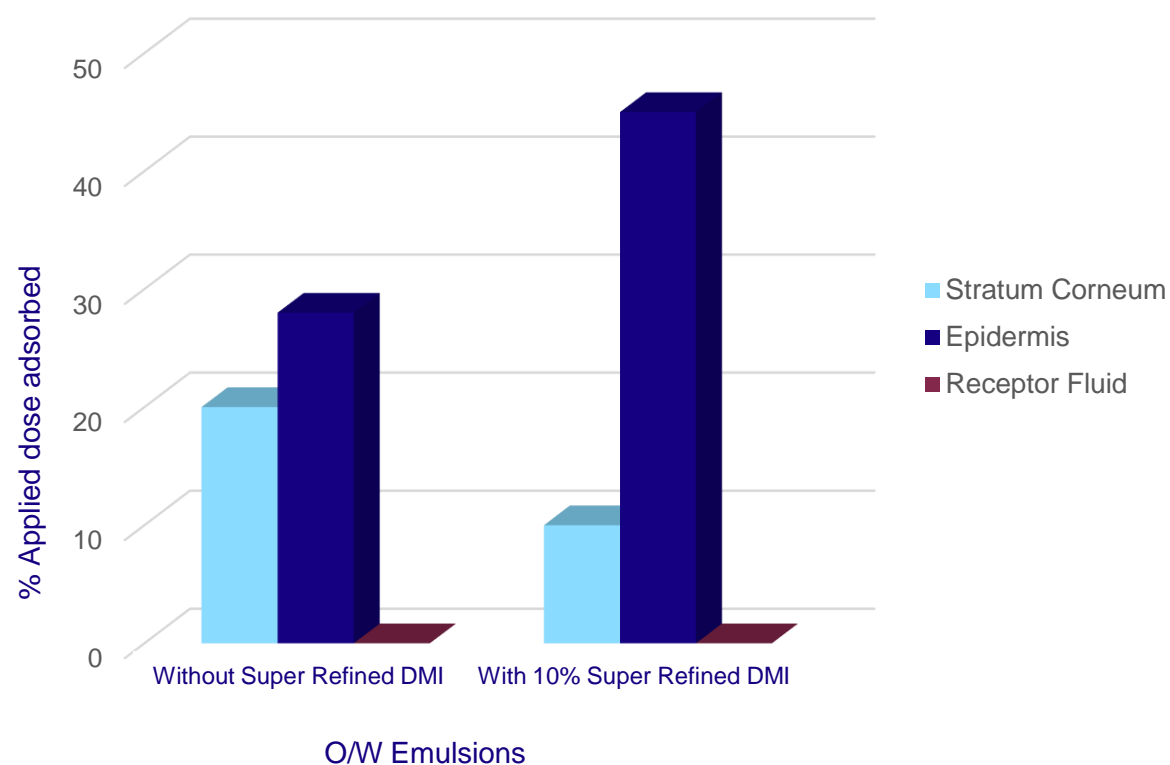


Super Refined DMI samples with and without 1% Benzocaine at 9 weeks 50°C

Super Refined™ DMI

Smart science to improve lives™

### Enhancing penetration with a topical API



CRODA



# Case study topical oils and creams - increased penetration

*“Patients want increased action for pain relief from a topical application”*

## Technical barriers

- Oils and creams are the preferred format for CBD
- Require oil soluble permeation enhancers
- Ideally avoid water-based products, which will cause CBD to precipitate out

A close-up photograph of a person's shoulder and upper arm. A hand is holding a small white tube of cream and applying it to the skin. The person's other hand is resting on their shoulder. The image has a blue tint.

# Case study topical oils and creams - increased penetration

## Solutions

- **Super Refined™ IPM** is shown to increase permeation of pain relief drugs eg. lidocaine
- **Super Refined IPM** is oil soluble
- **Super Refined IPM** is an emollient and solvent with good spreading properties



# Case study topical oils and creams - increased penetration

## Pack claims

- ① Increased penetration

Super Refined™ DEGEE has also been shown to aid the penetration of lidocaine



# Croda oral delivery

## Forms

- Softgels
- Drops
- Sprays

It is estimated that around 80% of drugs are consumed orally. Orally administered medication can have an unpleasant bitter taste, before and after digestion; thus causing poor consumer compliance.

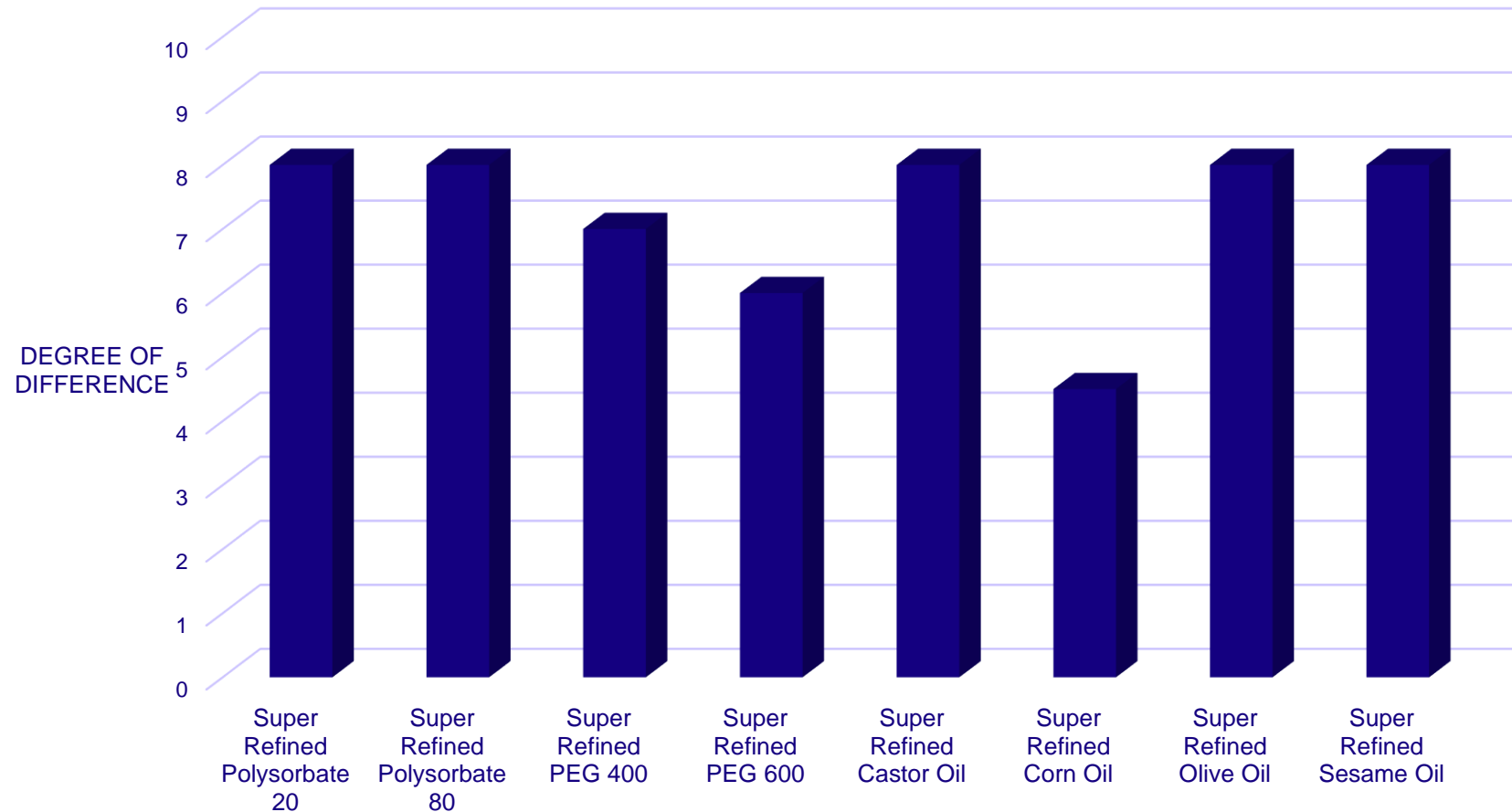
## Key products

- **Super Refined™ Sesame Oil, Super Refined Corn Oil** offer a low taste consumer benefit
- **Super Refined Polysorbate 80** offers an extreme difference in taste compared to standard **Polysorbate 80**

*Our formulation experts can provide inspiration to support your formulation development.*



# Croda oral delivery





# Case study oral solutions - reducing colours and flavours

*“Consumers want to avoid artificial colours,  
flavours and preservatives”*

## Technical barriers

- Many excipients have a bitter or unpleasant taste
- Anti-oxidants such as BHT are undesirable
- API's in multi use solutions can degrade, reducing shelf life
- Consumers are looking for no, or very low, levels of colour and flavours



# Case study oral solutions - reducing colours and flavours

## Solutions

- **Super Refined™ Corn Oil** has a reduced taste compared to their standard grade counterparts.
- Super Refined excipients offer non-preserved (BHT free) grades with reduced risk of API and excipient degradation
- Most Super Refined excipients are colourless, reducing the need for colours




# Case study oral solutions - reducing colours and flavours

## Pack claims

- ① Reduced sweeteners
- ② Reduced flavours
- ③ No artificial colours

Super Refined™ excipients have been shown to improve stability with ~70% of APIs

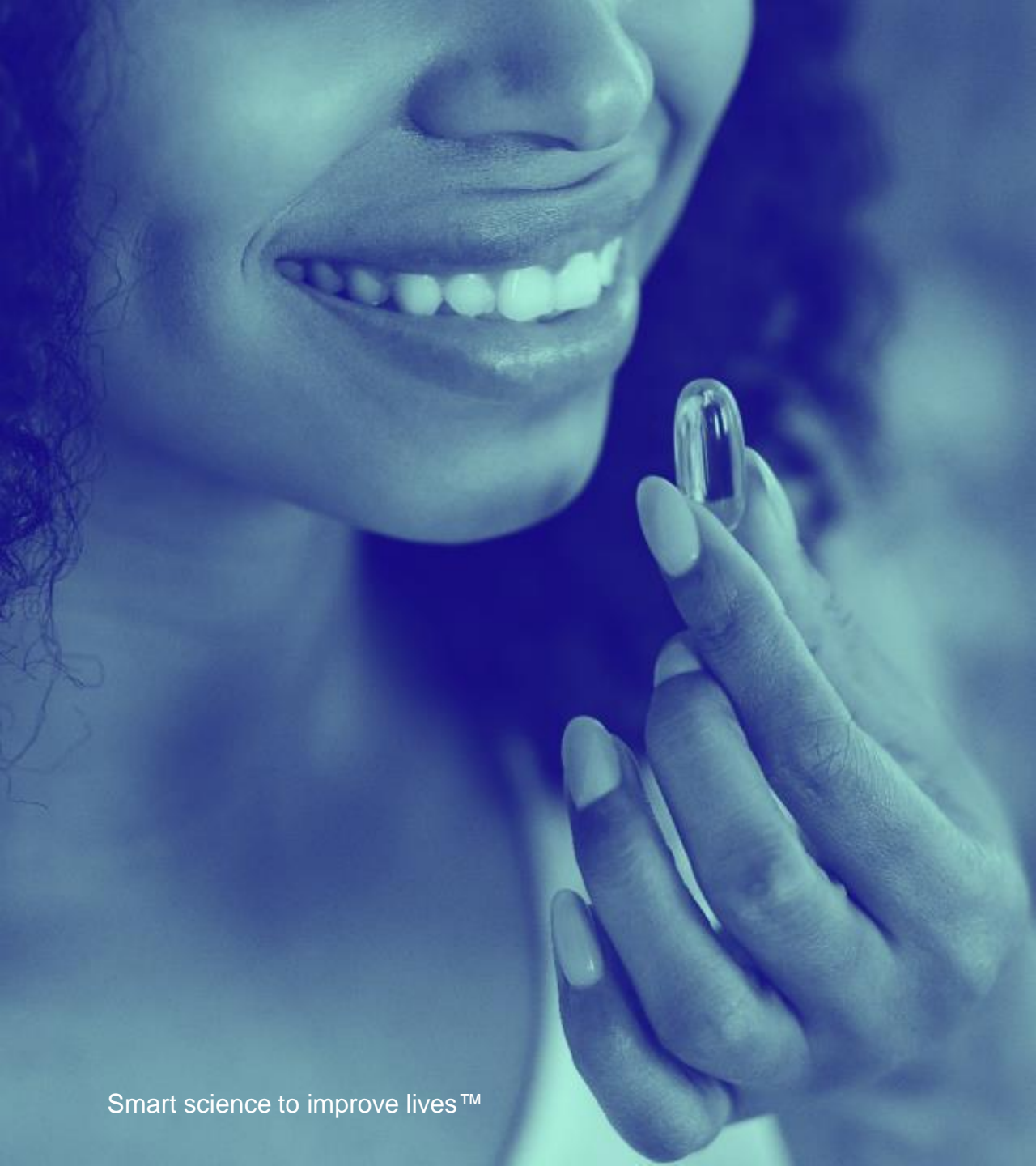
A photograph of a young woman with dark, curly hair, smiling warmly. She is holding a clear glass of water in her right hand and a single, clear, oval-shaped capsule in her left hand. The background is softly blurred, suggesting an indoor setting with natural light. The entire image has a light blue tint.

# Case study oral capsules – faster delivery

*“Patients want faster action for pain relief”*

## Technical barriers

- Tableted products only release the product based on the API solubility and the tablet disintegrants
- Liquid solutions in capsules increase the risk of API degradation
- Liquid solutions can struggle to dissolve the therapeutic API dose
- Significant development time in formulations



# Case study oral capsules – faster delivery

## Solutions

- **Super Refined™ P35 Castor Oil** disperses the API for rapid absorption and action
- **Super Refined™ PEG 400** acts as the main solvent to successfully dissolve the therapeutic dose
- Croda's in house oral liquid dose formulation knowledge used to get to the right answer, fast



# Case study oral capsules – faster delivery

## Pack claims

- ① Fast action
- ② Liquid capsule

Super Refined™ PEG 400 reduces the risk of  
cross linking in soft gel capsules



# Why work with us?

Create **tailored excipient solutions** directly in partnership with our scientists.



Tackle your stability challenges with **unparalleled purity excipients** across all administration routes.



**Formulate and troubleshoot faster** by working with our scientific experts during your development.



Prioritise **sustainability** and **integrity** by choosing Croda.

## Croda Pharma

We want to help you grow your product brand by offering **quality ingredients** developed for the **oral and topical Consumer Health** and markets.

With our ingredients, your products can **champion the noisy Consumer Health market.**

Let's talk.



### Non-warranty

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