hydrocurc™

ONE OF THE MOST BIOAVAILABLE CURCUMIN OF THE MARKET

solchem®

hydrocurc™

APPLICATION

Hydrocurc™ is indicated to help in the following conditions:

- Arthritis for its anti-inflammatory action.
- Loss of appetite.
- Digestive disorders:
  - Pain and bloating.
  - Dyspepsia.
  - Postprandial feeling of fullness.
  - Irritable bowel syndrome (IBS).
  - Peptic ulcers.
  - Colon inflammation.
- Liver and biliary disorders.
- Jaundice.

Other applications include:

- Conjunctivitis.
- Wound healing in topical use.
- Urinary tract infections.
- Menstrual troubles.

TURMERIC

The use of turmeric or curcuma (*Curcuma longa L.*) is dating back nearly 4,000 years old in the Vedic culture of India, where it was used as a culinary spice and had religious significance. Turmeric is used as food, in cosmetics and medicine.

Turmeric is widely used as a spice in cooking South Asia and the Middle East and gives to curry its distinctive flavour and yellow color. Currently, it has been identified more than 100 components present in the rhizome of turmeric, being essential oil and curcuminoids the major components. Curcuminoids, which include curcumin, demetoxy-curcumin, 5'-metoxy-curcumin and dihydro-curcumin, are the compounds responsible for orange colour of turmeric and are considered as natural anti-oxidants.

Besides the antioxidant action, curcuminoids also present anti-inflammatory, hepatoprotective, choleretic, carminative and antimicrobial activity. These properties have been demonstrated at scientific level both in vitro and in vivo studies and in clinical trials. Most of them have been performed on the digestive tract and intestine, for example in the treatment of irritable bowel syndrome and colon inflammation.

Other studies have demonstrated the efficacy of turmeric as anti-inflammatory in the treatment of rheumatoid arthritis.

In general, the doses used or extrapolated to human consumption is about 1.2 g of curcumin per day.

THE PROBLEM OF CURCUMINOIDS BIOAVAILABILITY

Despite the beneficial properties of curcuminoids, different studies have shown that curcumin is low bioavailable even at very high oral doses, focusing its reduced water solubility as the main cause. Beside this, there is the added problem that curcumin, when absorbed, is transformed into derivative conjugates that are rapidly eliminated by the body. Therefore, the benefits of turmeric are only obtained when the concentration of curcumin in plasma is very high to ensure that its derivatives can reach the target tissues to achieve their action before they are withdrawn out of our body.

Several proposals have been tried to resolve the low bioavailability of curcuminoids:

- Using turmeric extracts highly concentrated in curcuminoids, typically 95% of curcuminoids.

- Adding black pepper extract rich in piperine to turmeric since different studies states that piperine increases curcuminoids bioavailability.

However, neither of these two strategies is able to ensure an effective concentration of curcuminoids and its derivatives in plasma, nor the enough circulation time to ensure its effectiveness, before is eliminated by the body.

TECHNOLOGIES TO INCREASE CURCUMINOIDS BIOAVAILABILITY

Given the problems of solubility, absorption and distribution of curcuminoids in plasma, in the last years several methodologies have been developed to ensure the maximum bioavailability of these actives.

All these methods are based on turmeric extracts highly concentrated in curcuminoids included in a matrix of different nature, according to the technology applied. This matrix ranges from simple processes of microencapsulation to the development of more complex structures such as liposomes. However, according to the technological process applied, this matrix can represent from 40 to 80% of the finished product, which means that the product will contain from 20 to 40% of turmeric extract, which often makes to recommend several grams as effective doses.

Many of the products obtained by these technologies have demonstrated in different trials their capacity to increase the assimilation and bioavailability of curcuminoids. Depending on the recommended dose of each brand, some marketed products offer maximum absorption values of curcumin ranging from 20 to 600 ng per ml of plasma.

LipiSperse™: A TECHNOLOGY THAT INCREASES THE BIOAVAILABILITY OF LIPOSOLUBLE SUBSTANCES

Liposoluble compounds have low solubility in the non-aqueous gastrointestinal environment. These substances follow the same route of intestinal absorption than other fatty substances that are consumed, that implies the presence of bile salts for emulsion in the form of micelles.

Micellas increase the transport through the gastrointestinal tract. Therefore, when liposoluble compounds are taken, the usual practice is to ingest with a fat source to aid absorption.

As mentioned above, in recent years it has been developed a variety of delivery systems which have improved low bioavailability of curcumin. These different proposals have shown different responses to the degree of bioavailability of curcuminoids. Research done by Pharmako Biotechnologies laboratory has resulted in the development of **LipiSperse™** technology that, up to date, ensures the highest bioavailability of fat-soluble substances.

LipiSperse™ It is a new system designed to increase the dispersion of crystalline lipophilic agents in aqueous environments.

LipiSperse™ is a patented and clinically-validated self micro-emulsifying drug delivery system (SMEDDS), specifically designed to increase the bioavailability of lipophilic actives. **LipiSperse™** technology achieves a microemulsion solution through a physical process that creates micelles formed by lipid compounds with the property to be soluble in water. This system leads to an increased bioavailability of liposoluble active ingredients.

LipiSperse™ is a lipid-based formulation that self-assemble in contact with an aqueous phase forming a colloidal system administration of micelles with a diameter measurable in particles of micron range.

The effectiveness of technology **LipiSperse™** has been validated scientifically by:

- Analysis of laser light darkening, including the determination of the size and volume of the particles.
- Pharmacokinetic tests in humans, ensuring the release of the active compound systemically.

This technology makes possible to solubilize lipids for liquid forms, but also offers liposoluble products in powder form that:

- Maintains its dilution capacity in aqueous media.
- Maintains the same bioavailability in liquid form.
- Has good fluidity without orming lumps or sticky aggregates.
- Provides a high content of active ingredients.

LipiSperse™ technology has been used to develop **Hydrocurc™** as the most soluble and bioavailable turmeric in the market.

HYDROCURC™: A TURMERIC EXTRACT COLD WATER DISPERSIBLE (CWD)

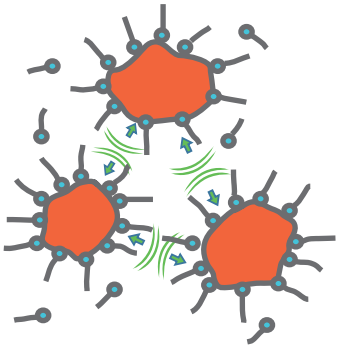
Unlike other turmeric powders in the market developed with technologies that incorporate from 40 to 80% of carrier, **Hydrocurc**™ contains 90% turmeric extract and only 10% of **LipiSperse™** matrix, which provides more than 80% of curcuminoids fully dispersible in water.

Currently, this value is the highest one that can be obtained with respect to other technologies of dispersion or solubilization of curcuminoids in aqueous media.

In aqueous environments such as the stomach, curcumin particles presented **Hydrocurc**™ disperse freely. This net effect subsequently results in higher bioavailability.

Hydrocurc™ is a trade mark of turmeric that supplies the most water dispersible curcuminoids quantity and, therefore, the most bioavailable in the market as demonstrated by pharmacokinetic studies

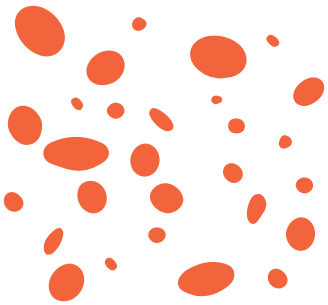
Repulsion forces between particles prevent agglomeration / aggregation, allowing curcuminoids **Hydrocurc™** having an optimum dispersion of the particles in water.



Optimum dispersion:

Wide effective surface area

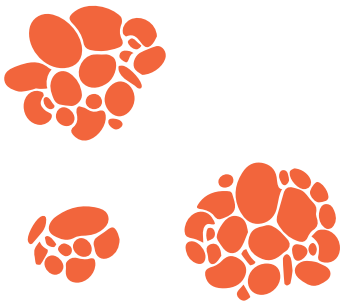
= increased Bioavailability

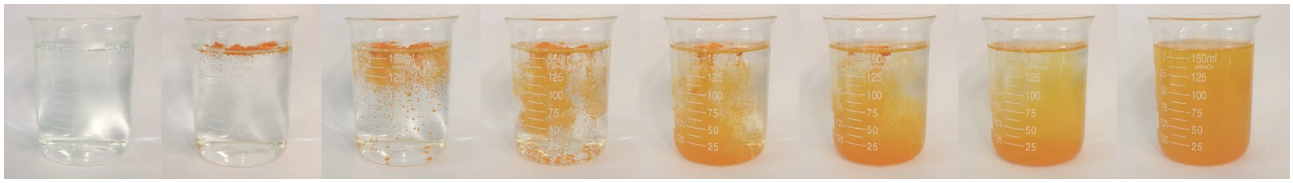


Limited dispersion:

Reduced effective surface area

= limited Bioavailability





PHARMACOKINETICS OF HYDROCURC™

Several pharmacokinetic studies comparing the plasma concentration of curcuminoids present **Hydrocurc**™ respect to conventional turmeric extracts with 95% curcuminoids have been carried out.

The objective of these studies were to evaluate the effectiveness of technology **Lipisperse™** in increasing blood curcumin concentration for a period of 24 hours.

One study was conducted with the participation of 18 volunteers in a cross and parallel randomized double-blind trial over 24 hours of follow-up. In this study, the same dose of turmeric was administered as **Hydrocurc**™ or as standard turmeric extract. Both treatments provided a total dose of 750 mg curcuminoids (80% curcumin, 17% demethoxycurcumin -DMC-, 3% bisdemetoxicurcumina -BDMC-).

Table 1 and Figures 1 to 4 show the results of bioavailability of curcuminoids, calculated as Cmax and AUC in volunteers who consumed **Hydrocurc**™ or the standard turmeric extract. The results indicate that **Hydrocurc**™ produced a significant increase in each curcuminoid value (curcumina, DMC and BDMC) and in total curcuminoids compared to the standard turmeric.

The parameter AUC (area under the curve) reflects the total amount of curcuminoids that reach the systemic circulation and is the most important measure of bioavailability.

In this regard, it is important to note that the control of total plasmatic concentration indicated in Table 1 and Figure 1 is for a total of 6 hours of curcuminoids permanence in plasma, much greater than 2 hours permanence than other studies of bioavailability carried out with other commercial turmerics.

Table 1.
Bioavailability of curcuminoids in volunteers following ingestion of 750 mg of total curcuminoids (**Hydrocurc**™ or standard turmeric extract)

	Hydrocurc™ (750 mg total curcuminoids)		Turmeric d.e. 95% curcuminoids (750 mg total curcuminoids)	
Curcuminoids	C_{max} (ng/mL)	AUC (ng/mL)	C_{max} (ng/mL)	AUC (ng/mL)
Curcumin	692 ± 124	1521 ± 201	215 ± 224	742 ± 248
DMC	93 ± 73	250 ± 64	22 ± 15	100 ± 29
BDMC	24 ± 11	86 ± 12	8 ± 5	33 ± 9
Total curcuminoids	**807**	**1857**	**245**	**875**

AUC: Area under the curve of plasma concentrations of curcuminoids.
C_{max}: maximum absorption peak after 1h in the case of **Hydrocurc™** and after 2 h in the case of standard turmeric.

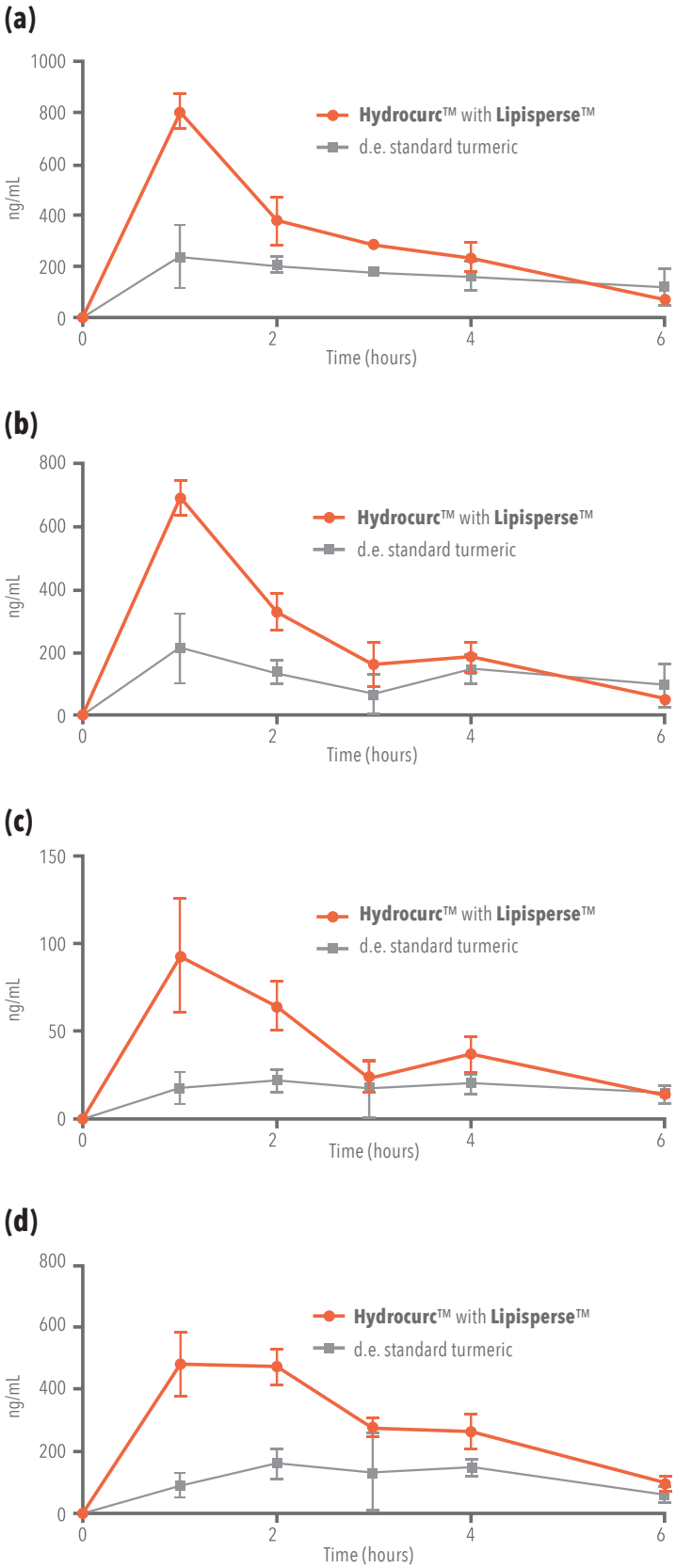


Figure 1.
Hydrocurc™ pharmacokinetics after single dose in volunteers versus pharmacokinetics of a standard dry extract of turmeric. **(a)** total curcuminoids, **(b)** curcumin **(c)** demethoxycurcumin (DMC) and **(d)** bisdemethoxycurcumin (BDMC).

HYDROCURC™ OVER OTHER TRADEMARKS

While there is no clinical study comparing all turmerics in the market among themselves, the truth is that all commercial brands have their own pharmacokinetic studies comparing its bioavailability respect to standard turmeric extracts.

However, recently it has been published a study that evaluates the pharmacokinetics of commercial curcumin compared to other commercial formulations (Sidney J. *et al*., 2018).

Referencing this study, Table 2 shows the results obtained from the publication when comparing different brands for the parameters: recommended dose, Cmax curcumin and AUC curcumin.

In addition, Table 2 include the values for **Hydrocurc™** for the same parameters and an additional column comparing AUC curcumin/mg recommended does, that is not shown in the original table of the article.

According to this comparison, CurQfen mark shows the highest bioavailability of the recommended dose, followed by **Hydrocurc™** and other brands by descending order of results.

If we calculate the maximum absorption of curcumin given by recommended dose (Cmax / recommended dose), **Hydrocurc™** presents the highest score with a score of 0.87, followed by BioCurc with 0.71 and CurQfen 0.579 (data not shown in table).

Taking together the values of maximum absorption (Cmax), concentration over time (AUC), recommended doses and curcuminoid content in the product, **Hydrocurc™** is one of the most bioavailable Turmerics in the market.

Table 2.

Comparison of the results of absorption maximum curcumin (Cmax and AUC) and recommended dose bioavailability (AUC / dose) in various commercial Turmerics respect to **Hydrocurc™**.

Commercial Name	Recommended (*) dose (mg)	Amount of curcumin / recommended dose (mg)	C_{max} curcumin (ng/mL) (*)	AUC curcumin (ng.h/mL) (*)	AUC curcumin/mg recommended dose
CurQfen	1000	391	579	2274	2.27
Hydrocurc™	**800**	**648**	**692**	**1521**	**1.90**
BCM-95	2000	1718	573	3588	1.79
BioCurc	400	64,6	282	351	0.88
Meriva	2000	376	207	1336	0.67
Theracurcmin	1500	182	231.5	693	0.46
CurcuWIN	1567	376	34.9	380	0.24
Cavacurmin	2000	371	87	389	0.19
Longvida	650	163	22.4	95.3	0.15

AUC: Area under the plasma concentration curve of curcumin.
Cmax: absorption peak of curcumin. (*) Sidney J. *et al*., 2018

SAFETY

The use of turmeric as a spice and food is safe. Up to date, no studies in animals or humans has discovered toxic effects associated with the use of turmeric.

RECOMMENDED DOSE

A dose of 400 to 800 mg of **Hydrocurc**™ shared into two doses is recommended.

PRESENTATIONS

Hydrocurc™ it can be used in the formulation:

- Vegetable or hard gelatin capsules.
- Powder formulations to solubilize in stick, sachet or pot.
- Liquid presentations in vials or syrups.

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