

**BIOAVAILABILITY OF CURCU-GEL™ Softsules®
Containing (BCM-95™ SG)**

A HUMAN STUDY

Study Conducted at:

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Introduction

Curcuma longa L (Zingiberaceae) is a perennial herb that measures up to 1 M high with a short stem, distributed throughout the tropical and subtropical regions of the world, and widely cultivated in India and China and other Asian countries. The powdered rhizome, called turmeric, has been in continuous use for its flavoring and digestive properties. Traditional Indian medicines use the powder against biliary disorders, anorexia, cough, diabetic wounds, hepatic disorders, rheumatic disorders sprains and swellings caused by injury, and sinusitis¹. Traditional Chinese medicine uses curcuma in diseases associated with abdominal pain. Turmeric is an integral part of religious ceremonies of the Hindus. Curcumin (1,7-(4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dione) is the major component of turmeric and is responsible for the varied bioactivities of turmeric.

The most studied pharmacological action of curcumin is its anticancer properties and curcumin is presently under clinical trials. There are more than 500 reports on the chemopreventive, anticancer, antiangiogenic, and apoptotic properties of curcumin. Curcumin's anticancer effects have been demonstrated in virtually every organ of the human body

Despite a broad array of biological activities, the bioavailability in humans remains poor, seriously curtailing the benefits derivable from curcumin. Research at Arjuna

Natural Extracts Ltd indicated that blending a portion of the turmeric essential oil with curcumin could significantly enhance the bioavailability of curcumin.

The present study was conducted to validate this effect in humans.

Test substances:

1. Curcumin capsule (500mg hard gelatin)
2. Curcu-Gel™ Softsules® containing 250 mg of BCM-95™ SG

Subjects: Four human volunteers were selected between the age group 20-30 for clinical trial on the bioavailability.

Study Procedure: Under a controlled study the Volunteers were advised not to consume any food containing turmeric a day prior to the test and during the test, fasting blood was collected from all the volunteers. This was the control. The volunteers were advised to take **4 capsules of Curcumin (500mg X 4)** as a single dose at 7 a.m. All of them were provided with similar food on the day of the test. Blood samples were collected at 1hr, 2hr, 3hr, 5hr, 7hr and 10hr after taking the capsules and were kept deep-frozen till analyses.

After one week, the protocol was repeated with Curcu-Gel™ Softsules® containing BCM-95™ SG Softsules® containing BCM-95™, Fasting blood was collected from all the volunteers. This was the control. The volunteers were allowed to take **8 capsules of Curcu-Gel™ Softsules® containing BCM-95™ SG (250mg X 8)** as a single dose.

Extraction of Curcumin from blood samples: The blood was extracted exhaustively with ethyl acetate –LR grade (10ml X 4 times). The ethyl acetate fractions were pooled and concentrated to dryness. This was then made up to 10ml with methanol and used for HPLC analysis

Estimation of Curcumin using HPLC: Samples were analyzed on HPLC (Shimadzu), equipped with UV detector using a C-18 column (250X4.6mm; 5 μ m particle size) from Phenomenex. Twenty micro liter of the sample was injected and the mobile phase consisted of methanol that was applied isocratically. The flow rate was adjusted to 1.0ml/min. and the detection wavelength was 420 nm. Peaks were assigned by comparison with standard curcumin (Sigma Chemical Company, USA). The retention time of standard curcumin, as well as from the sample under the above conditions was 3.3 minutes

Results: The results obtained for volunteers A, B, C and D are shown in Table 1, Table 2, Table 3 and Table 4 respectively. Table 5 shows the average values. Concentrations of curcumin, expressed as micromoles per liter of blood at different time intervals after consumption of Curcumin/Curcu-Gel™ Softsules® were plotted against time. Figure 1, Figure 2, Figure 3 and Figure 4 show the graphs drawn using the values of the Curcumin and Curcu-Gel™ Softsules® for the volunteers A, D, C and D respectively. Figure 5 is the graph obtained for the average values. The areas under the curcumin curve were calculated for both Curcumin (control) and Curcu-Gel™ Softsule®. Ratio of such areas was used to evaluate the enhancement of bioavailability of Curcu-Gel™ Softsules®.

Conclusion: From the respective areas under the curcumin curve for reference curcumin and Curcu-Gel, the bioavailability of Curcumin from Curcu-Gel™ Softsules® was found to be 8.2 times higher compared to normal curcumin, on the average.

In the case of Curcu-Gel™ Softsules® a slight increase in blood concentrations is observed, at low level concentrations between 7 hours and 10 hours, which could be due to a delayed absorption of any small fraction of unabsorbed drug in the intestine during a second food intake.

Time (hours)	Curcumin in blood ($\mu\text{moles/L}$)	
	Curcumin	Curcu-Gel™ Softsules® containing BCM-95™ SG
0	0	0
1	0.003024	0.093727
2	0.035802	0.207346
3	0.075916	0.421049
5	0.023717	0.115663
7	0.00812	0.015688
10	0.007193	0.22454

Table 1 : Blood concentrations of Curcumin and Curcu-Gel™ Softsules® ($\mu\text{moles/L}$) at specified periods after administration on volunteer A

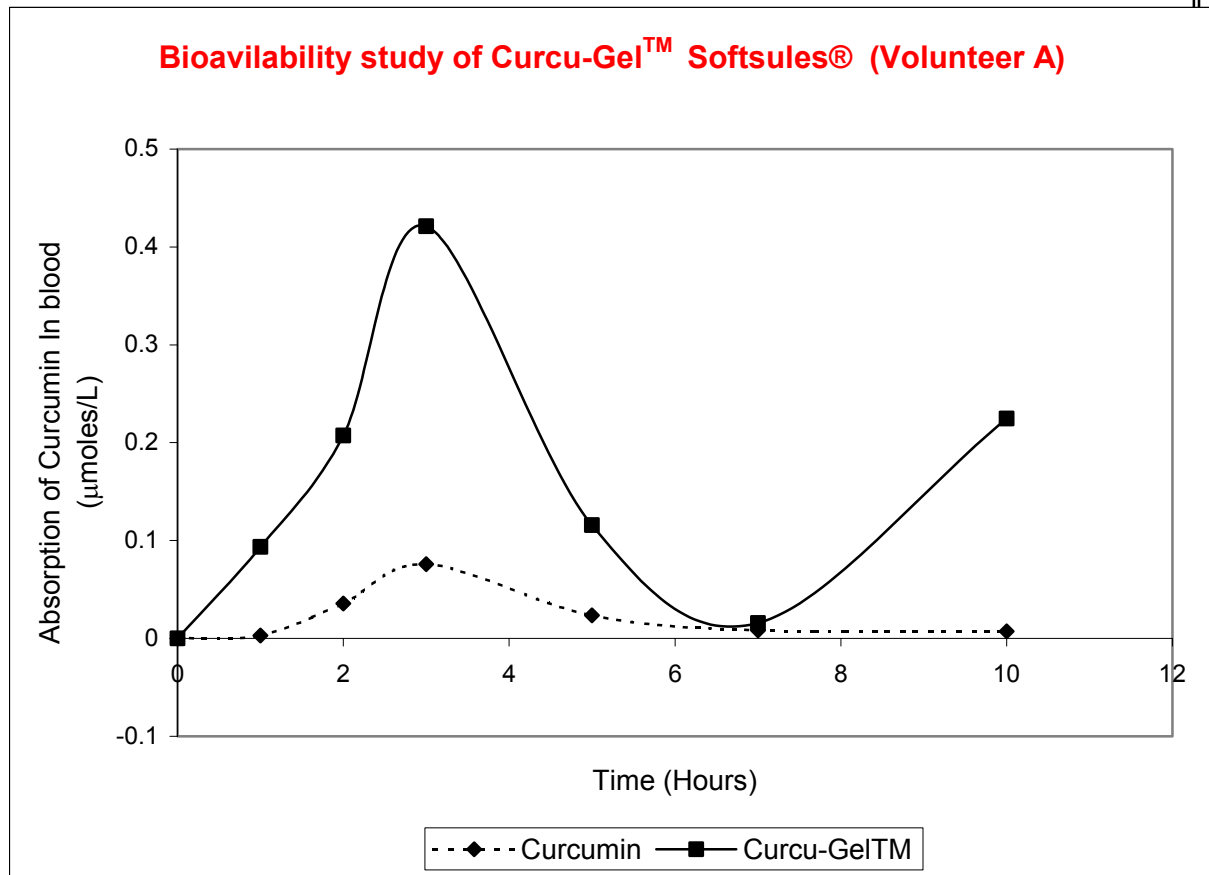


Figure 1: Bioavailability of curcumin and Curcu-Gel™ Softsules® for Volunteer A

Time (hours)	Curcumin in blood ($\mu\text{moles/L}$)	
	Curcumin	Curcu-Gel™ Softsules® containing BCM-95™ SG
0	0	0
1	0.008586	0.07434
2	0.049996	0.431122
3	0.020119	0.287089
5	0.012054	0.03446
7	0.01699	0.035486
10	0.014001	0.102223

Table 2 : Blood concentrations of Curcumin and Curcu-Gel™ Softsules® ($\mu\text{moles/L}$) at specified periods after administration on volunteer B

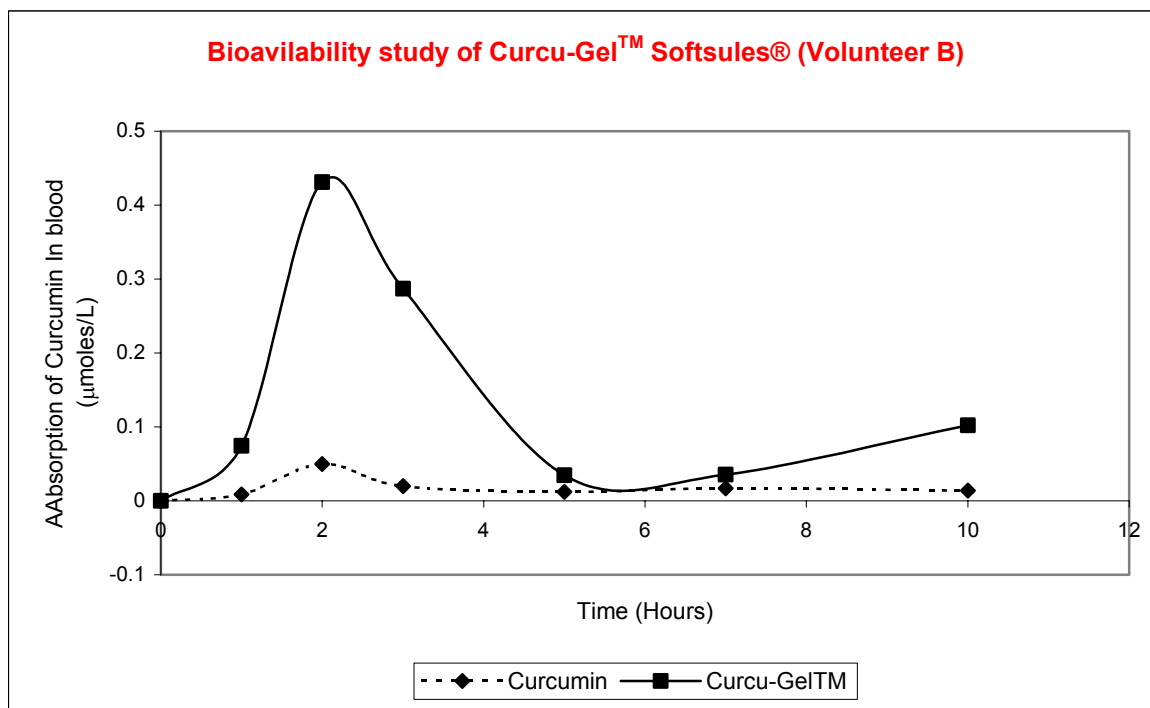


Figure 2: Bioavailability of Curcumin and Curcu-Gel™ Softsules® for Volunteer B

Time (hours)	Curcumin in blood ($\mu\text{moles/L}$)	
	Curcumin	Curcu-Gel™ Softsules® containing BCM-95™ SG
0	0	0
1	0.005115	0.356395
2	0.102076	0.397653
3	0.025686	0.446777
5	0.041046	0.871328
7	0.024017	0.025575
10	0.019341	0.078414

Table 3: Blood concentrations of Curcumin and Curcu-Gel™ Softsules® ($\mu\text{moles/L}$) at specified periods after administration on volunteer C

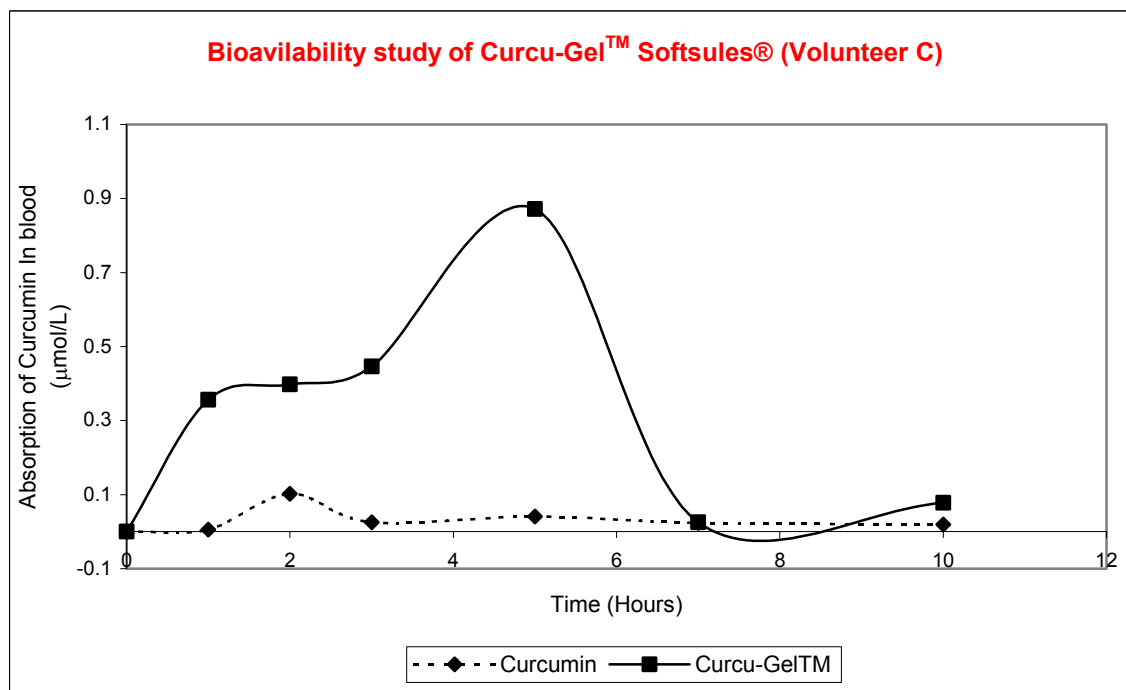


Figure 3: Compiled bioavailability of Curcumin and Curcu-Gel™ Softsules® for Volunteer C

Time (hours)	Curcumin in blood ($\mu\text{moles/L}$)	
	Curcumin	Curcu-Gel™ Softsules® containing BCM-95™ SG)
0	0	0
1	0.004372	0.684169
2	0.171207	0.584983
3	0.020151	0.169626
5	0.022324	0.206618
7	0.00538	0.045458
10	0.008346	0.111757

Table 4: Blood concentrations of Curcumin and Curcu-Gel™ Softsules® ($\mu\text{moles/L}$) at specified periods after administration on volunteer D

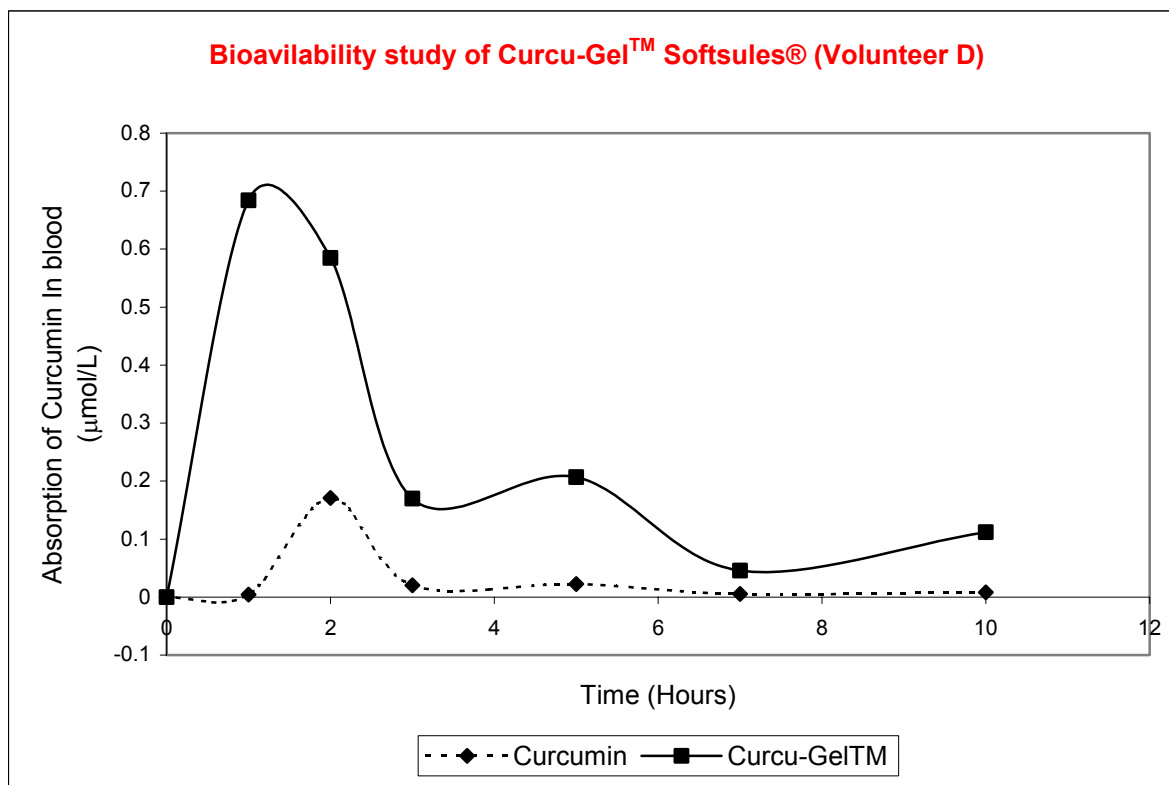


Figure 4: Bioavailability of Curcumin and Curcu-Gel™ Softsules® for Volunteer D

Time (hours)	Curcumin in blood ($\mu\text{moles/L}$)	
	Curcumin	Curcu-Gel™ Softsules® containing BCM-95™ SG)
0	0.0000	0.0000
1	0.0053	0.3022
2	0.0898	0.4053
3	0.0355	0.3311
5	0.0248	0.3070
7	0.0136	0.0306
10	0.0122	0.1292

Table 5 : Compiled blood concentrations of Curcumin and Curcu-Gel™ Softsules® ($\mu\text{moles/L}$) at specified period after administration on four volunteers

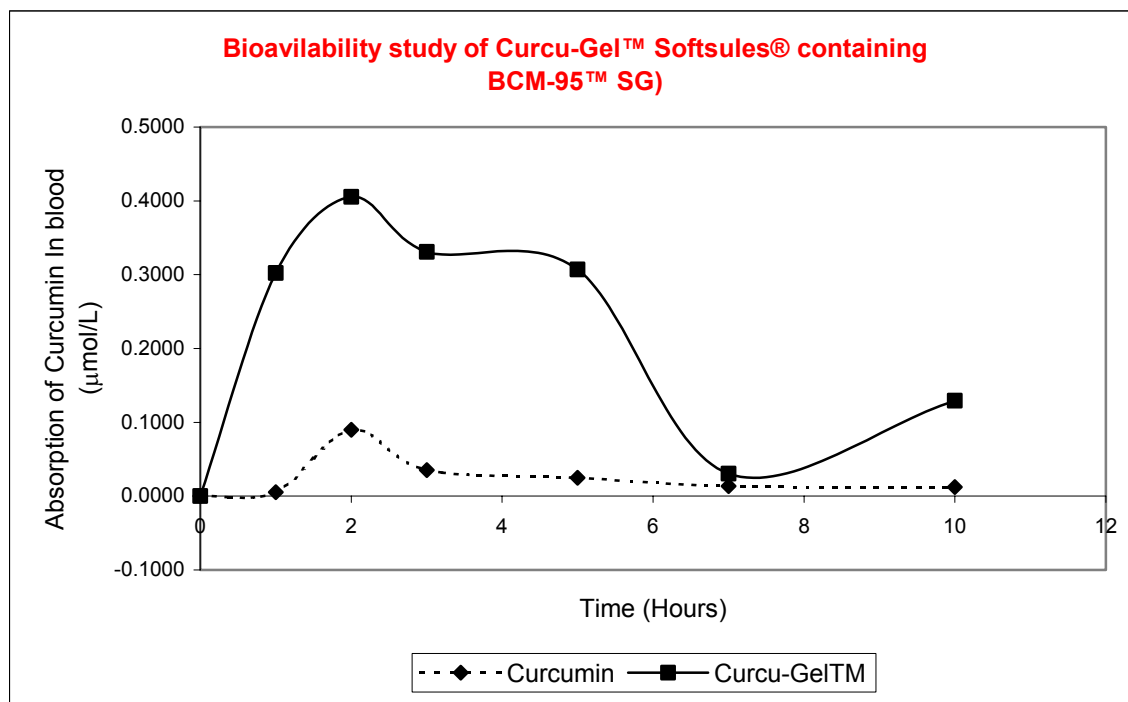


Figure 5: A compiled bioavailability chart of Curcumin and Curcu-Gel™ Softsules® containing BCM-95™ of four volunteers

Statistical Analysis

Blood concentrations of Curcumin and Curcu-Gel™ Softsules® (μmoles/L) at specified periods after administration on four volunteers

Time hours	Curcumin in blood (μmoles/L)							
	Curcumin				Curcu-Gel™ Softsules® containing BCM-95™ SG)			
	A	B	C	D	A	B	C	D
0	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
1	0.0030	0.0086	0.0051	0.0044	0.0937	0.0743	0.3564	0.6842
2	0.0358	0.0500	0.1021	0.1712	0.2073	0.4311	0.3977	0.5850
3	0.0759	0.0201	0.0257	0.0202	0.4210	0.2871	0.4468	0.1696
5	0.0237	0.0121	0.0410	0.0223	0.1157	0.0345	0.8713	0.2066
7	0.0081	0.0170	0.0240	0.0054	0.0157	0.0355	0.0256	0.0455
10	0.0072	0.0140	0.0193	0.0083	0.2245	0.1022	0.0784	0.1118

Standard deviation

Time hours	Curcumin	Curcu-Gel™ Softsules® containing BCM-95™ SG)
0	0.0000	0.0000
1	0.0021	0.2471
2	0.0531	0.1343
3	0.0235	0.1112
5	0.0104	0.3314
7	0.0074	0.0111
10	0.0049	0.0563

The standard deviations of the blood concentrations expressed in μmoles/L falls within acceptable limits.