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INCREASED SOLUBILITY AND STABILITY OF CURCUMIN IN LACTIC ACID

J.Venkateshwar Rao[1] & M.N.A.Rao[2]*

[1*]Principal, Talla Padmavathi College of Pharmacy, Urus, Kareemabad, Warangal-506009, India
[2]Research Head, Divis Research Foundation – Hyderabad
*Corresponding Author Email: pharmacyvenkat@gmail.com

Research Article

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ABSTRACT

The solubility and the stability of curcumin increases to a significant extent in the solution containing lactic acid. There was two fold increase in the solubility in 60% lactic acid at a pH 7.0 and twenty fold increase at pH 1.5 when compared to aqueous solution at pH 7.0. Almost similar increase in half life was observed. The ($t_{1/2}$) of aqueous solution, at pH 7.0, was 5.7 hr., In the presence of 60% lactic acid, it increased to 11.9 hr., at pH 7 and to 174 hr., at pH 1.5.

KEYWORDS: curcumin, Solubility and Stability, Lactic Acid.

INTRODUCTION

Curcumin (diferuloyl methane, CAS 458-37-7) from *Curcuma Longa* has many interesting pharmacological properties like anti-inflammatory and anticancer.[1] it has also been studied extensively for its various biochemical properties.[2] We have conducted several studies on free radical scavenging and other antioxidant properties of curcumin. [3-6]

Although, curcumin has high potential as a pharmacological agent, it has very poor solubility in water at the physiology pH. In the alkaline pH, its solubility increase due to salt formation. But in salt form, it undergoes very rapid degradation. Earlier attempts to use curcumin as a coloring agent in pharmaceutical formulations, like granulation and tableting, were unsuccessful due to its poor stability.[7]

The above facts prompted us to study different methods to increase the solubility and the stability of curcumin. In the present study, we describe the effect of lactic acid on the solubility and the stability of curcumin. The study showed, that in the presence of lactic acid, there was a significant increase in the solubility and the stability at neutral and acidic pH.

EXPERIMENTAL

Materials & Methods:

All the commercial samples of curcumin were found to be impure because of the presence of demethoxy and bisdemethoxy curcumin in small amounts. Hence, pure curcumin was chemically synthesized as described by Pabon.[8] The purity of the compound was confirmed by elemental analysis (C and H), m.p. and TLC. Lactic acid (DL) from S.D. fine chem. Ltd (extra pure). Other reagents were of analytical grade.

Determination of solubility: Excess amount of curcumin was added to a solution containing lactic acid at various concentrations in an airtight container. The solution was stirred at the room temperature for 3 hrs. and filtered. The absorbance of the filtrate was measured at 434nm (Shimadzu 240). From the absorbance, the concentration was determined using a standard plot.

The standard plot was obtained by measuring the absorbance of solutions containing various concentrations of curcumin in ethanolic solution (10%) at pH 7.0.

Stability Studies: The amount of curcumin present in the solution at various time intervals was measured up to 24 hrs or up to 6 hrs, if the degradation was rapid. First order rate constant (k) and half life ($t_{1/2}$) were calculated from the slope of the regression equation obtained between the log concentration and time.

RESULT AND DISCUSSION

The solubility of curcumin in solutions containing lactic acid in different proportion at pH 7.0 is given in the **(Fig. 1)**. The aqueous solubility of curcumin was found to be 7.5 µM. In the presence of lactic acid, up to 40% concentration, the solubility decreased. However, in 50% lactic acid solution, the solubility increased to an appreciable extent. Further increase in lactic acid proportion, resulted in further increase in curcumin solubility. About, 2.6 fold increase was achieved when compared to the aqueous solubility. In addition to the increase in the solubility, there was also increase in the stability of curcumin in lactic acid solution **(Table 1)**. The half life of curcumin in 80% lactic acid solution was found to be 13.3 hrs when compared to 5.7 hrs in aqueous solution we also studied the effect of pH on the solubility **(Fig. 2)**. There was an increase in the solubility at lower pH. at pH 1.5 the solubility in 60% lactic acid solution was found to be 443.8 µM compared to 20 µM at pH 7.0. Thus an increase of 20 fold could ve achieved at lower pH. However, the solubility also increased at pH 8.0, but it will not be of much use because of the rapid degradation at alkaline pH. Stability was found to be better at acidic pH **(Table.2)**. At pH 1.5 the half-life was found to be 174 hrs. Compared to 12 hrs at pH 7.0.

Thus the present study shows that the solubility of curcumin increases to a considerable extent in the presence of lactic acid. In addition to the solubility, the stability also increases to a significant extent. Earlier, lactic acid has been used to increase the solubility of drugs like haloperidol.[9] Another interesting property of lactic acid is its ability to reduce ferric ions to ferrous ions.[9] Our earlier studies have shown that curcumin is also capable of reducing ferric ions.[3] The significance of this synergistic action is to be further investigated. In conclusion, lactic acid can be a good solubilizing agent for curcumin and it can also potentiate some of the actions of curcumin.

TABLE 1: Stability of curcumin in solutions containing various concentrations of lactic acid at pH 7.*

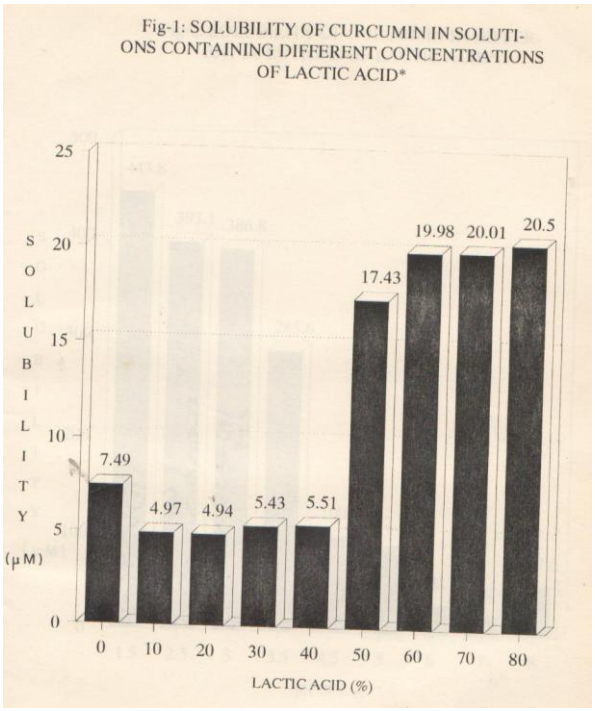
Lactic acid %	Slope X 10^{-4}	r	k(hrs^{-1}) X 10^{-4}	$t_{1/2}$ (hrs^{-1})
0 (100% water)	87.6	0.96	84.0	5.74
20	7.5	0.91	17.3	6.66
40	6.6	0.98	15.0	7.70
60	4.2	0.99	9.6	11.90
80	3.7	0.99	8.7	13.28

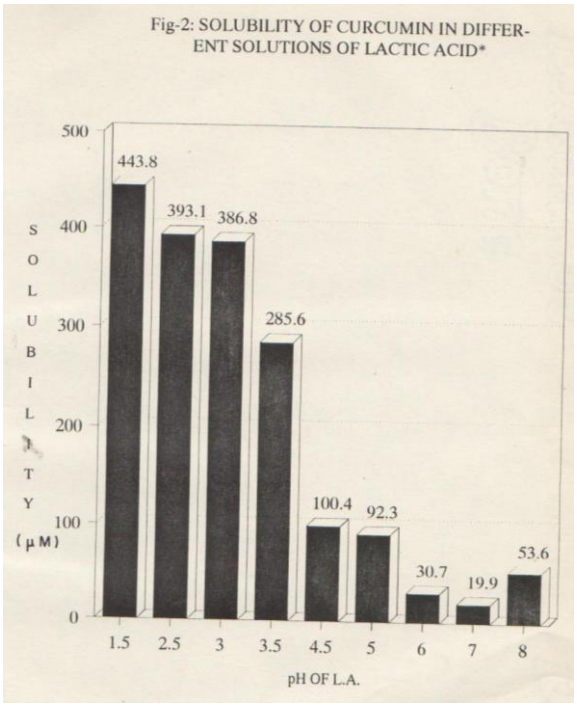
* Stability was determined from a plot of log concentration against time. r is correlation coefficient for the regression, k(hrs^{-1}) is the first order rate constant and $t_{1/2}$ is the half-life.

TABLE 2: Stability of curcumin in 60% lactic acid solution at acidic and neutral pH.*

pH	Slope X 10^{-5}	r	k(hrs^{-1}) X 10^{-4}	$t_{1/2}$ (hrs^{-1})
1.5	2.8658	0.95	0.66	174.0
3.4	5.2974	0.96	1.22	94.4
7.0	41.687	0.98	9.60	11.9

* Stability was determined as given in **Table 1**.





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*Address for the Correspondence:
J.Venkateshwar Rao*
Principal,
Talla Padmavathi College of Pharmacy,
Urus, Kareemabad,
Warangal-506009, India.
Tel: +91-9849945165
Email: pharmacyvenkat@gmail.com