

# Bioavailability of Liposome-Encapsulated Ascorbic Acid (Vitamin C)

February 2020

## 1. Study Objective

To evaluate the bioavailability of a liposomal vitamin C supplement (liposomal) compared to a non-liposomal vitamin C supplement (standard).

## 2. Methods

The current study was a two-group, randomized controlled trial of the effect of liposomal versus standard vitamin C supplements on plasma ascorbic acid (AA) levels measured for six hours after administration of a single dose.

### 2.1. Participants

Twenty metabolically healthy participants enrolled in the study. They were randomly and evenly assigned to either the liposomal or standard supplementation group. Participant exclusion criteria included:

- Age <20 and >50 years
- Any diagnosis of chronic condition(s)
- BMI outside of the normal category range (18.5-24.9kg/m<sup>2</sup>)
- Presence of acute illness
- Use of drugs or dietary supplements on a frequent and/or mandatory basis

### 2.2. Active Substances

#### a. Liposomal Product:

Purazell Liposomal Vitamin C (8mL/1,000mg)

Company:

Roh Vegan am Limit / Patrick Strobach

Sandstrasse 104

40789 Monheim am Rhein

#### b. Standard Product:

Amazon Element Vitamin C (1 tablet/1,000mg)

Distributed by:

Amazon Fulfillment Services, Inc

410 Terry Avenue N., Seattle, WA 98109

### 2.3. Dosage and Blood Collection

An oral dose of 1,000mg of liposomal or standard vitamin C supplement was administered to fasted participants. Plasma was collected at baseline (B0), 60 minutes (T1), 180 minutes (T2), and 360 minutes (T3) after administration. Plasma was then measured for ascorbic acid levels (AA) using High Performance Liquid Chromatography (HPLC) techniques at the laboratories of Surya Research Clinics.

### 2.4. Statistics

Pharmacokinetic parameters are presented as max concentration ( $C_{max}$ ), time to max concentration ( $T_{max}$ ), area under the curve from baseline to the final measurement ( $AUC_{0-t}$ ) and oral bioavailability value (OBV).  $AUC_{0-t}$  was calculated using the trapezoidal rule and OBV was determined as liposomal  $AUC_{0-t}$  / standard  $AUC_{0-t}$ .

Between group and within group analyses were conducted to determine significant changes in plasma AA levels. A two-way ANOVA with Tukey's comparison of means was performed to determine the difference between groups in mean plasma AA levels at B0, T1, T2, and T3. A one-way repeated measures ANOVA with Tukey's pairwise comparisons was used to determine the within group changes in mean plasma AA levels from B0 to T3 in both the liposomal and the standard group.

### 3. Results

All enrolled participants completed the study. Participants were in their late twenties, predominately male and had a healthy BMI and blood pressure. Participant anthropometric data is presented in *Table 1*. A graphical representation of plasma AA levels over time is available in *Figure 1*.

$C_{max}$  was 2.20mg/dL in the liposomal group and 0.83 mg/dL in the standard group. The liposomal group had a  $T_{max}$  of 360 minutes while the  $T_{max}$  in the standard group was 60 minutes.  $AUC_{0-t}$  was 8.02 mg\*hr/dL in the liposomal group and 4.69mg\*hr/dL in the standard group resulting in an OBV of 1.71. These data are presented in *Table 2*.

A two-way ANOVA was conducted that examined the effect of supplement type (treatment) and time of blood draw on plasma AA levels. There was a statistically significant interaction between the treatment and time of blood draw on the plasma AA levels,  $F(3,71) = 11.28$ ,  $p = 0.000$ ,  $R^2 = 66.86\%$ . Simple main effects analysis showed that the liposomal group had significantly higher levels of plasma AA levels at T2 ( $p = 0.000$ ) and T3 ( $p = 0.000$ ) when compared to the standard group. There were no significant differences between groups at B0 ( $p = 1.000$ ) or T1 ( $p = 0.416$ ). The results from the comparisons of means test are presented in *Table 3*.

A one-way repeated measures ANOVA was conducted to examine the effects of time on supplementation within both the liposomal and standard groups. There was a statistically significant effect of time on plasma AA levels in the liposomal group,  $F(3,36) = 16.94$ ,  $p = 0.000$ ,  $R^2 = 58.54\%$ . Tukey's comparison of means test revealed a significant increase in plasma AA levels from, B0-T2 ( $p = 0.000$ ), B0-T3 ( $p = 0.000$ ), T1-T2 ( $p = 0.046$ ), and T1-T3 ( $p = 0.002$ ). There were no significant differences between plasma AA levels from B0-T1 ( $p = 0.067$ ) and T2-T3 ( $p = 0.613$ ). These results are presented in *Table 4*. There were no significant increases over time in the standard group ( $F(3,35) = 1.84$ ,  $p = 0.158$ ,  $R^2 = 13.63\%$ ). These results are presented in *Table 5*.

**Table 1. Participant Anthropometric Data**

	Liposomal <sup>ab</sup>	Standard <sup>ab</sup>
Age (years)	29.20 (5.00)	28.30 (6.70)
Females (%)	40.00	30.00
BMI (kg/m <sup>2</sup> )	21.20 (1.80)	21.40 (1.50)
Systolic BP (mmHg)	121.50 (16.30)	119.90 (18.50)
Diastolic BP (mmHg)	75.60 (8.40)	76.90 (6.80)

<sup>a</sup>Mean (SD)

<sup>b</sup>n=10

**Table 2. Pharmacokinetic Parameters**

	Liposomal	Standard
$C_{max}$ (mg/dL)	2.20	0.83
$T_{max}$ (minutes)	360.00	60.00
$AUC_{0-t}$ (mg*hr/dL)	8.015	4.685
OBV	1.71	

**Table 3. Between-Group Comparison of Mean Plasma AA Levels<sup>a</sup>**

Time Point	Standard <sup>bcd</sup>	Liposomal <sup>bcd</sup>	Difference of Means <sup>c</sup>	95% Confidence Interval	T- Value	P-Value
<b>B0</b>	0.59 (0.07)	0.61 (0.08)	-0.02 (0.19)	-0.63, 0.58	-0.12	1.000
<b>T1</b>	0.83 (0.10)	1.24 (0.20)	-0.41 (0.19)	-1.00, 0.19	-2.12	0.416
<b>T2</b>	0.82 (0.09)	1.90 (0.17)	-1.08 (0.19)	-1.68, -0.48	-5.61	0.000*
<b>T3</b>	0.73 (0.07)	2.20 (0.21)	-1.48 (0.20)	-2.09, 0.86	-7.47	0.000*

<sup>a</sup> Data analyzed using two-way ANOVA with Tukey Comparison of Means<sup>b</sup> n=10<sup>c</sup> Mean (SE)<sup>d</sup> Unit mg/mL

\* P-Value &lt;0.05 is statistically significant

**Table 4. Change in Mean Plasma AA Levels Over Time in Liposomal Group<sup>ab</sup>**

Time Point	Difference of Means <sup>c</sup>	95% Confidence Interval	T-Value	P-Value
<b>T1-B0</b>	0.63 (0.24)	-0.03, 1.28	2.56	0.067
<b>T2-B0</b>	1.29 (0.24)	0.63, 1.95	5.29	0.000*
<b>T3-B0</b>	1.59 (0.24)	0.93, 2.25	6.52	0.000*
<b>T2-T1</b>	0.67 (0.24)	0.01, 1.32	2.73	0.046*
<b>T3-T1</b>	0.97 (0.24)	0.31, 1.62	3.96	0.002*
<b>T3-T2</b>	0.30 (0.24)	-0.36, 0.96	1.23	0.613

<sup>a</sup> Analyzed using Tukey's pairwise comparisons<sup>b</sup> n=10<sup>c</sup> Mean (SE)

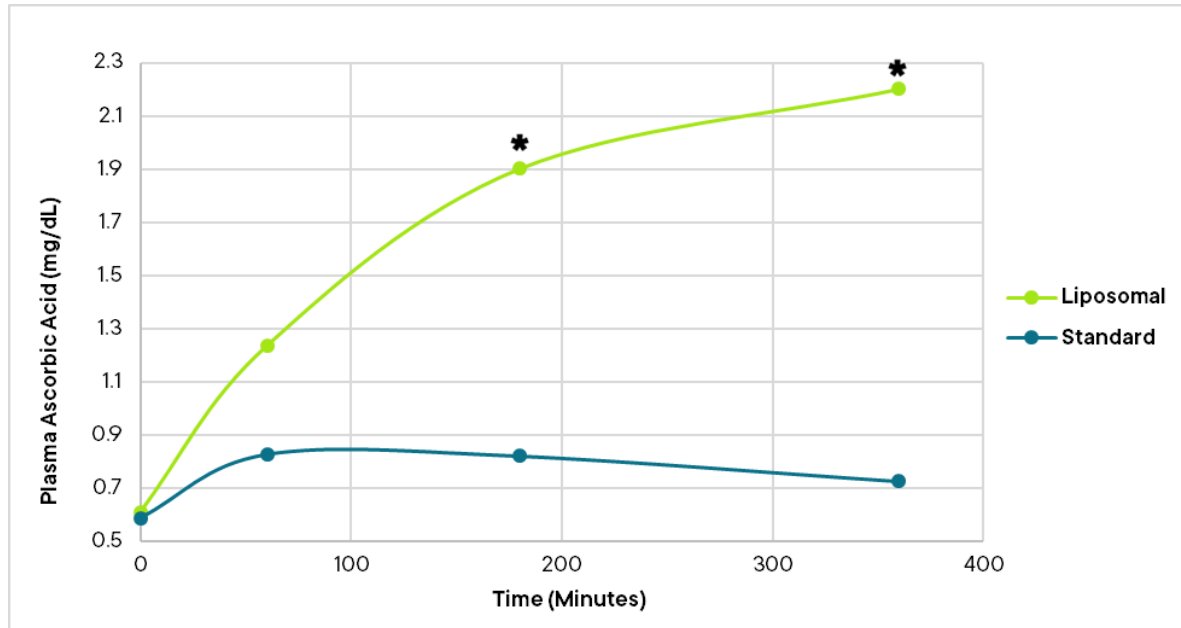
\* P-Value &lt;0.05 is statistically significant

**Table 5. Change in Mean Plasma AA Levels Over Time in Standard Group<sup>ab</sup>**

Time Point	Difference of Means <sup>c</sup>	95% Confidence Interval	T-Value	P-Value
<b>T1-B0</b>	0.24 (0.12)	-0.08, 0.56	2.06	0.187
<b>T2-B0</b>	0.24 (0.12)	-0.08, 0.55	2.00	0.209
<b>T3-B0</b>	0.14 (0.12)	-0.19, 0.46	1.15	0.664
<b>T2-T1</b>	-0.01 (0.12)	-0.32, 0.31	-0.06	1.000
<b>T3-T1</b>	-0.10 (0.12)	-0.43, 0.22	-0.86	0.827
<b>T3-T2</b>	-0.10 (0.12)	-0.42, 0.23	-0.80	0.855

<sup>a</sup> Analyzed using Tukey's pairwise comparisons<sup>b</sup> n=10<sup>c</sup> Mean (SE)

\* P-Value &lt;0.05 is statistically significant



**Figure 1.** Plasma AA levels over time after administration of 1,000mg vitamin C supplement in liposomal or standard form  
\* Indicates a significant difference ( $p < 0.05$ )

## 4. Conclusion

The liposomal vitamin C supplement significantly raised plasma AA levels after 180 and 360 minutes when compared to a standard vitamin C supplement. The AUC for the liposomal supplement was greater than that of the standard formulation resulting in an oral bioavailability value of 1.71. This suggests that the amount absorbed from a single dose of liposomal vitamin C is higher and thus the liposomal formulation is more bioavailable than a standard supplement at the same dose. These study results are aligned with previous studies on liposomal vitamin C bioavailability showing that it is more bioavailable than standard supplements.<sup>1</sup> Study limitations include a small sample size, a limited number of blood draws, and the lack of a placebo group. Future studies should consider the addition of a placebo group, a larger sample and blood draws for a full 24 hours after supplement administration.

## References

1. Davis JL, Paris HL, Beals JW, et al. Liposomal-encapsulated Ascorbic Acid: Influence on Vitamin C Bioavailability and Capacity to Protect against Ischemia-Reperfusion Injury. *Nutr Metab Insights*. 2016;9:NMI.S39764. doi:10.4137/NMI.S39764

## Acknowledgements

Study conducted in collaboration with:  
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