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Vitamin C Transport Pathways

> Vitamin C is a hydrophilic (water soluble) compound which exists in two forms in vivo – ascorbic acid (ASC, the reduced form) and Dehydroascorbic acid (DHA, the oxidised form). As there is almost constant intra-cellular cycling between the two, both forms contribute to the total body pool of Vitamin C.[1]

> As Ascorbic acid is a water-soluble compound, passive diffusion is only thought to occur minimally and very slowly even under the influence of a large concentration gradient.[1]

> Ascorbic acid transport is sodium dependent via Sodium Vitamin C Co-transporter1 (SCVT1) molecules, whereas DHA absorption is glucose dependent via GLUT1 or 3 transport molecules. SCVT1 facilitated absorption is an active transport process whereas GLUT1/3 transporters utilise facilitated diffusion which is a passive transport mechanism.[1]

> Absorption takes place through the apical brush border membrane of the small intestine.[1]

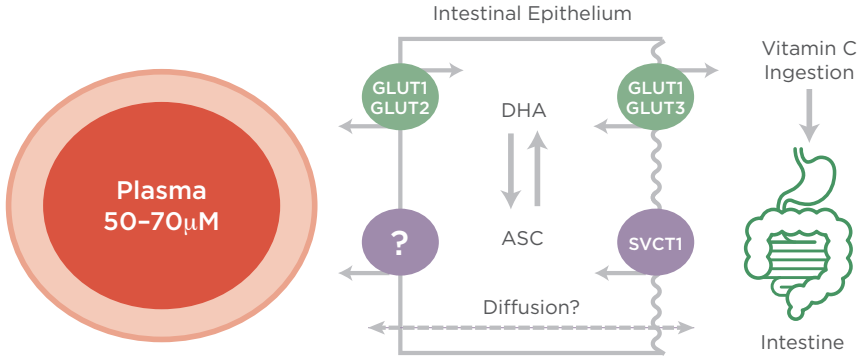
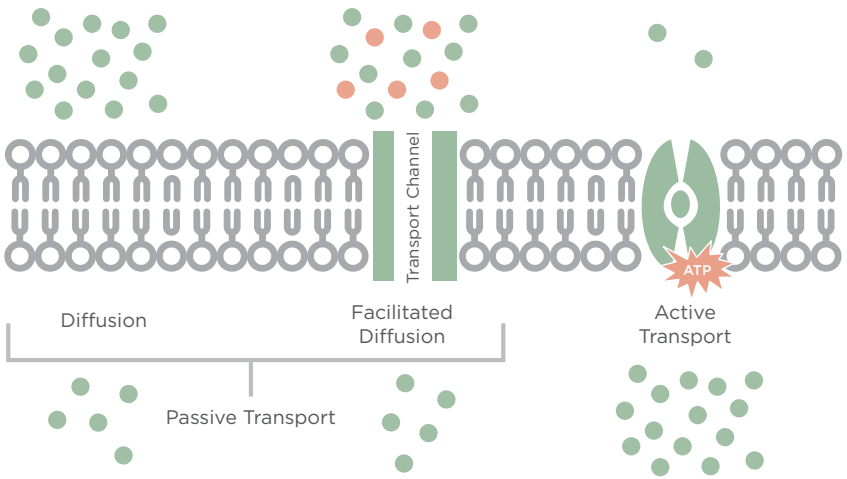


Figure 1.

Ingested vitamin C (vitC) is absorbed across the intestinal epithelium primarily by membrane transporters in the apical brush border membrane, either as ascorbate (ASC) by sodium-coupled active transport via the SVCT1 transporter or as dehydroascorbic acid (DHA) through facilitated diffusion via GLUT 1 or GLUT3 transporters. Once inside the cell, DHA is efficiently converted to ASC or transported to the blood stream by GLUT1 and GLUT2 in the basolateral membrane, hereby maintaining a low intracellular concentration and facilitating further DHA uptake. ASC is conveyed to plasma by diffusion, possibly also by facilitated diffusion through volume-sensitive anion channels or by yet unidentified active transporters; the precise efflux mechanisms remain unknown.

Figure 2. Different types of Vitamn C transport



WATER BASED PATHWAYS

> The pathway that provides the most significant amounts of vitamin C transport is the SVCT1 pathway, followed by facilitated diffusion via GLUT1/3 transporters with passive diffusion providing minimal amounts.[1]

> Active transport utilising the SVCT1/s transporters is saturable and therefore limited. Doses of around 1000mg once daily can saturate SVCT1.[4,5] SVCT1 activity is also further downregulated when intestinal vitamin C levels are high.[4]

> Absorption rates therefore drop as the administered dose is increased.[1,4,5]

> Large doses that don't take these absorption challenges into account are eliminated via the kidneys at rates of up to 50%.[5]

LIPID BASED PATHWAYS

> Lipid based technology utilising phospholipids and fat-soluble vitamin forms allow additional absorption via alternative transport pathways such as the lymphatic system via chylomicron formation.[1,2,3]

> Lipid based vitamin forms have been shown to:

1. increase plasma exposure to ascorbic acid by around 35% after four hours.[1,2]
2. produce higher circulating ascorbic acid concentrations tha n the non-lipid-based forms.[2]
3. maintain higher tissue retention times for 24 hours after supplementation.[3]
4. create a greater reduction of inflammatory and oxidative stress indicators.[3]

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WHICH ALTERNATIVE PATHWAYS ARE UTILISED WITH LIPID-BASED VITAMIN C SUPPLEMENTS?

Lipophilic medicines are preferentially taken up by the intestinal lymphatic system, so manipulating both hydrophilic and lipophilic therapeutic compounds to display the characteristics of lipids (as is the case with liposomes and PureWay-C™), increases lipophilicity and routes these medicines towards intestinal lymphatic transport systems.[6] Oral absorption via passive diffusion is also possible when utilising substances of a low molecular weight.

PUREWAY-C™

ALTERNATIVE PATHWAY UTILISED: LYMPHATIC.
Also enhances intestinal uptake via direct incorporation into cell membranes (phospholipid incorporation).

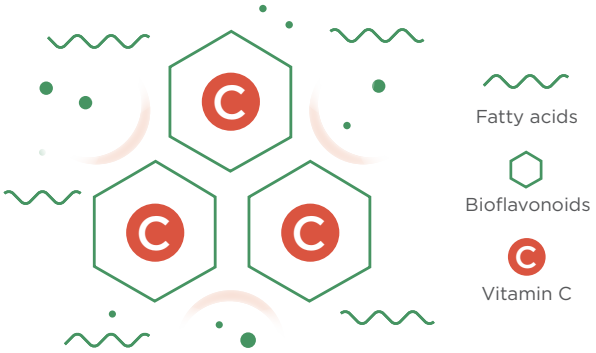

Figure 3.

Pureway-C™: Bioflavenoids help protect ascorbic acid whilst fatty acids offer aternative transport mechanism.

PureWay-C™ is an innovative lipid-based formulation containing a blend of ascorbic acid, bioflavonoids and fatty acids (phospholipids) to optimise bioavailability, cellular uptake, and tissue distribution and retention of Vitamin C.

The bioflavonoids in the formulation help to protect the ascorbic acid from oxidative damage, keeping it stable and active in the system for prolonged periods of time.

The fatty acid portion facilitates cellular absorption and enables the normally water-soluble ascorbic acid access to biological tissues. It acts as an alternative "ascorbic acid carrier" enhancing intestinal absorption, tissue distribution and cellular uptake kinetics of vitamin C.

Both in vivo and in vitro clinical research has been conducted on PureWay-C™ and its efficacy has been documented in reliable peer-reviewed medical journals.

Normal plasma levels of vitamin C are generally greater than 0.3mg/dl 3. Supplementation with 1000mg (the saturable dose for SVCT1 transporters) of a standard water-based vitamin C supplement such as calcium ascorbate results in plasma levels of 1.12mg/dl, and 1000mg of the water-soluble ascorbic acid results in plasma levels of 1.64mg/dl after 2 hours. The addition of a lipid-based technology such as PureWay-C™ results in plasma levels almost 94% higher than calcium ascorbate and 32% higher than ascorbic acid at 2.17mg/dl at the same 1000mg dose after the same time period. This has been shown to coincide with greater reductions in both plasma C-reactive protein and Oxidised LDL proteins after supplementing with PureWay-C™.[3]

LIPOSOMAL C

ALTERNATIVE PATHWAY UTILISED: ORAL (BUCCAL AND SUBLINGUAL) AND LYMPHATIC

Liposomal forms of vitamin C encase or enmesh the vitamin C in a phospholipid sphere. As cell membranes are also made of phospholipids, Liposomal medicines have the ability to mimic the physiology of a cell membrane and deliver medicines directly into the cell.

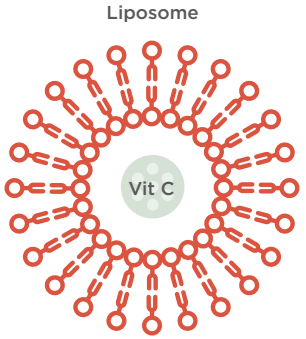

Figure 4.

Liposome with a hydrophillic medicine in the aqueous core.

Liposomal engineering increases the likelihood of lymphatic transport which avoids first-pass hepatic metabolism improving bioavailability, drug concentration and stability.[6,7] The utilisation of liposomal forms of Vitamin C increase plasma exposure to ascorbic acid by around 35% four hours after supplementation and produce higher circulating ascorbic acid concentrations than a water-based counterpart[1,2]

Substance breakdown and assimilation is one of the major functions of the oral mucosa. Compounds of low molecular weight such as liposomal medicines are able to be absorbed into the blood vessels via the oral epithelial tissues.[9]

Medicine absorption via the mucous membranes in the oral cavity occurs via passive diffusion into the lipoidal tissue and can occur 3-10 times faster than swallowing a tabletted or capsulised therapeutic compound, whilst also bypassing first-pass hepatic metabolism which can further breakdown the ingested substance.[8,9] The medicine is absorbed into the reticulated vein underneath the tongue. It then travels through the facial veins, the internal jugular vein and the brachiocephalic vein before finally before finally entering the systemic circulation.[8]

References:

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