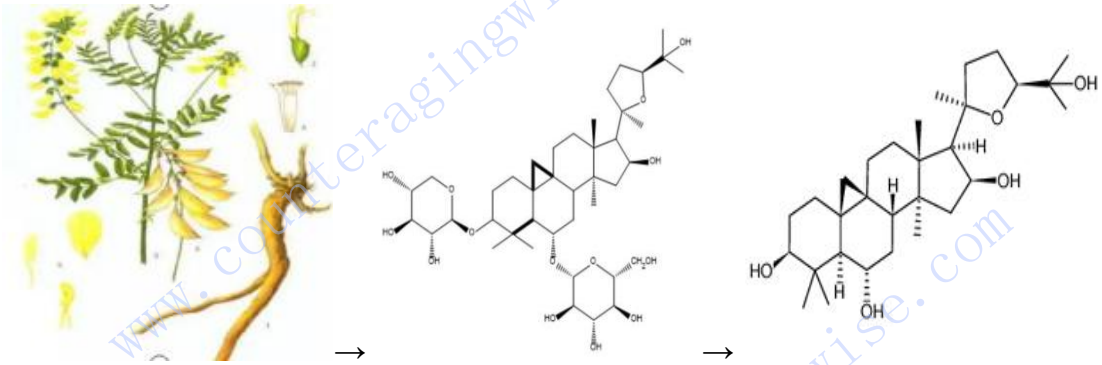
CAW® Water-Solubility Cycloastragenol Capsule

Formula

Astragalus polysaccharides is one of the active ingredients of Astragalus membranaceus root. Macromolecular Astragalus polysaccharides have many pharmacological effects, such as promoting immune organ function and antibody production, bidirectional blood glucose regulation, anti-tumor, antibacterial and antiviral effects [1-4]. Astragalus polysaccharide has excellent solubility in water, up to 100 mg/ml (>1:10).

Cycloastragenol is obtained by hydrolyzing natural Astragaloside IV from Astragalus membranaceus root under mild conditions. See *Figure 1.*



Astragalus membranaceous Astragaloside IV Cycloastragenol

Figure 1

Cycloastragenol is a telomerase activator, can delay the shortening of telomere by increasing the activity of telomerase. It could slow cell aging and allows cells to begin copying again. Therefore, Cycloastragenol is considered to have the effect of anti-aging[5].

Cycloastragenol is a tetracyclic triterpenoid, its solubility in water is extremely low, which is only 0.03mg/ml[6] (<1:10000). As its poor water-solubility, the bioavaiability of Cycloastragenol after oral administration is low too.

CAW® PLUS 300 is a new type of Cycloastragenol capsule. It is composed of high-purity macromolecular Astragalus polysaccharides and high-purity Cycloastragenol. Uses advanced preparation technology to combine the Astragalus Polysaccharide and Cycloastragenol together, so that the molecules of Cycloastragenol fully fit in Astragalus Polysaccharide molecules, and the combination in this way can increase the solubility of PLUS 300 in water. The solubility of Cycloastragenol in PLUS 300 is up to 10mg/ml in water, while the solubility of Cycloastragenol in ordinary Cycloastragenol capsules in water is only 0.03mg/ml.

Product Advantages

●CAW® Water-solubility Cycloastragenol Capsule is made of all natural ingredients with higher safety.

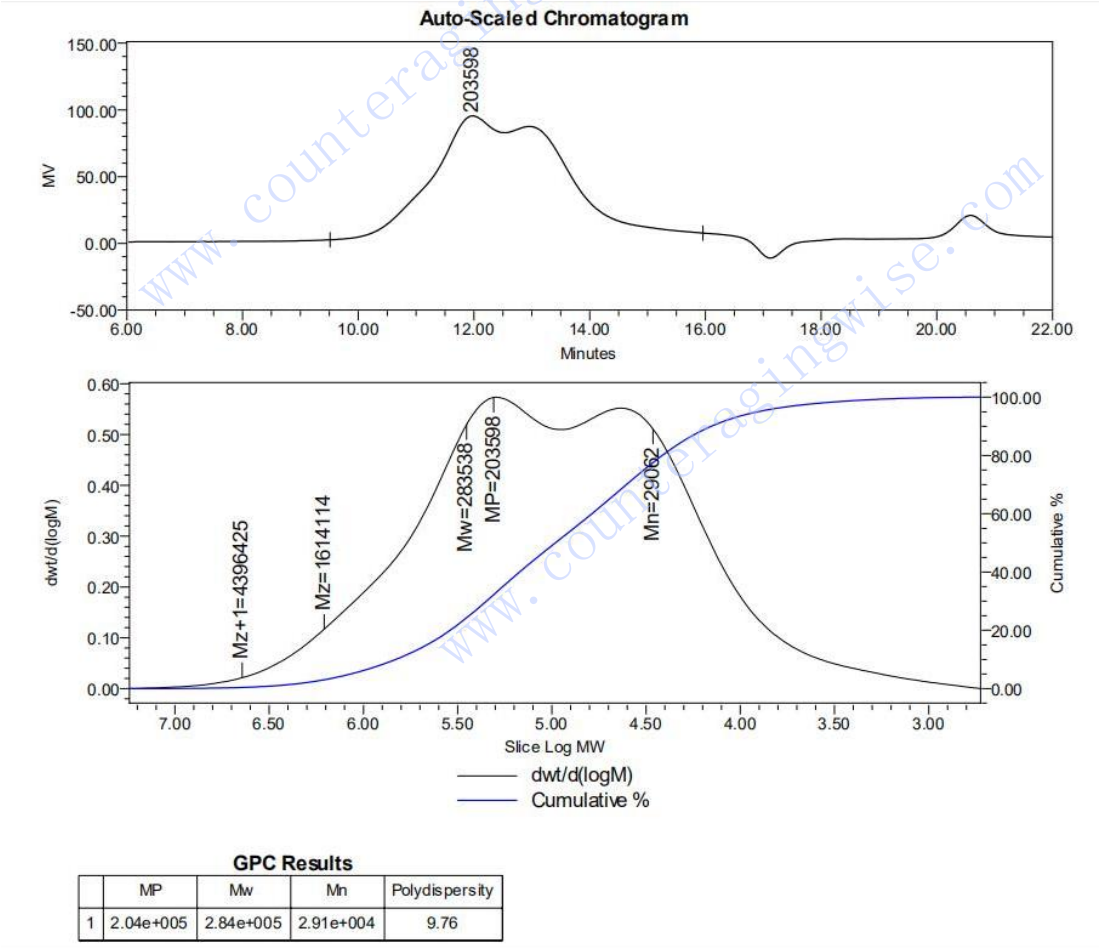
●The solubility of Cycloastragenol in water is significantly improved by the formula of Water-solubility Cycloastragenol Capsule.

●The dissolution rate of CAW® Water-solubility Cycloastragenol Capsule is significantly increased.

●The bioavailability of Cycloastragenol is significantly improved by the formula of Water-solubility Cycloastragenol Capsule.

●The optimization formula choose the true high purity Macromolecular Astragalus polysaccharides, which can help improve the function of Cycloastragenol.

The molecular weight distribution chromatogram of high purity Macromolecular Astragalus polysaccharides is as *Figure 2*.



GPC Results

	MP	Mw	Mn	Polydispersity
1	2.04e+005	2.84e+005	2.91e+004	9.76

Figure 2

The contents of CAW® Water-solubility Cycloastragenol Capsule are completely water-soluble, while the common Cycloastragenol couldn't be dissolved in water.

The pictures of them are compared as *Figure 3*.

The contents of common Cycloastragenol capsule and CAW® Water-solubility Cycloastragenol Capsule were both prepared with aqueous solution at the concentration of 10mg/ml, and the photos after dissolution were compared.

In *Figure 3*, the left side is the solution of common Cycloastragenol with concentration 10mg/ml. The solution is turbid and completely block the yellow background.

The right side of Figure 3 is the solution of CAW® Water-solubility Cycloastragenol with concentration 10mg/ml. The solution is clear and transparent, so that the yellow background can be clearly seen.

Figure 3

The Comparison of dissolution curves of common Cycloastragenol Capsule and CAW® Water-solubility Cycloastragenol Capsule.

Take Common Cycloastragenol capsule and CAW® Water-solubility Cycloastragenol Capsule, determine the in vitro dissolution of the two capsules, dissolution medium was Artificial Intestinal Juice(PH≥6.8), according to the provisions of the US Pharmacopoeia <711> DISSOLUTION. CAW® Water-solubility Cycloastragenol Capsule could be completely dissolved quickly with high in vitro dissolution. Its dissolution rate was 95% at 15min and more than 98% in 20min. While the dissolution rate of common Cycloastragenol capsule was slow and the dissolution rate in vitro was low yet. Its dissolution rate was 30% at 15 min, was 48% at 20 min.

The results of dissolution test showed that the in vitro dissolution of CAW® Water-solubility Cycloastragenol Capsule is significantly higher than that of common Cycloastragenol capsule.

The comparison of bioavailability between common Cycloastragenol capsule and CAW® Water-solubility Cycloastragenol Capsule.

The lipophilicity of Cycloastragenol is good, but its solubility in water is low, as a consequence, it is not easily absorbed by human body by oral administration due to the limit of solubility. Moreover, Cycloastragenol is widely metabolized in liver microsomes after being absorbed by human body. After 30 minutes of oral administration, the residual amounts of common Cycloastragenol is only 8.2% of the initial amount[7]. The low solubility and extensive first-pass effect greatly restrict the oral bioavailability of the product.

The dissolution rate of CAW® Water-solubility Cycloastragenol Capsule in vitro is much higher than that of common Cycloastragenol capsule, and the dissolution rate reached 98% in 20 minutes. Moreover CAW® Water-solubility Cycloastragenol Capsule can be rapidly dissolved in the gastrointestinal tract and quickly absorbed into the blood circulation by the human body. Compared with common Cycloastragenol capsule, the bioavailability of CAW® Water-solubility Cycloastragenol Capsule has been significantly improved ,see *Figure 4.*

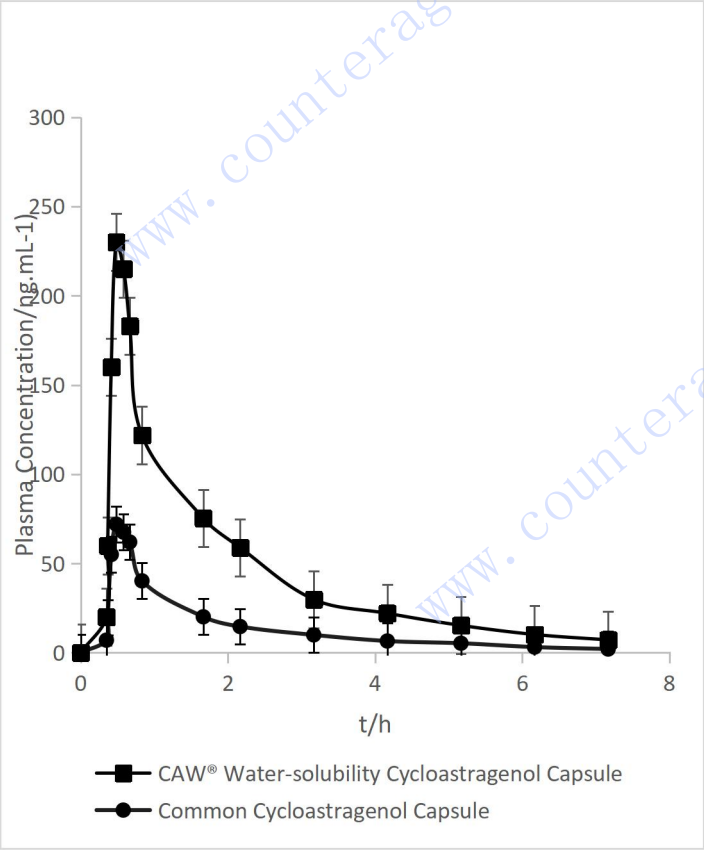


Figure 4

Figure 4 shows the plasma concentration-time curves of common Cycloastragenol capsule and CAW® Water-solubility Cycloastragenol Capsule in rats.

References

[1] Liu M, Qin J, Hao Y R, et al.Astragalus polysaecharide suppresses skeletal muscle myostatin expression in diabetes: involvement of ROS-ERK and NF-κB pathways[J]. Oxidative Medicine and Cellular Longevity, 2014, 1 (24): 497-507.

[2] Lian Y H, Xie L L, Chen M H, et al.Efects of an Astragalus polysaccharide and rhein combination on apoptosis in rats with chronic renal failure[J]. Evi-dence-Based Complementary and Alternative Medicine, 2014, 5(10): 862- 869.

[3] Zhu H Y. Gao Y H. Wang Z Y. et al. Astragalus polysaccharide suppresses the expression of adhesion molecules through the regulation of the p38 MAPK signaling pathway in human cardiac microvascniar endothelial cells after ischemia-reperfusion injury[J]. Evidence-based Complementary and Alternative M edidne: eCAM, 2013, 9(17): 493-501.

[4] Guo I, Bai S P, Zhao L et al. Astragalus polysaccharide injection integrated with vinorelbine and cisplatin for patients with advanced non-small cell lung cancer: effects on quality of life an survival[J]. Medical Ontology, 2012, 3 (29): 1656-1662.

[5] Bernardes de Jesus B, Schneeberger K, Vera E, Tejera A, Harley CB, Blasco MA.The telomerase activator TA-65 elongates short telomeres and increases health span of adult/old mice without increasing cancer incidence[J]. Aging Cell. 2011 Aug; 10(4): 604-21.

[6] Xiaoya LIU. Metabolism of Astragaloside IV and Cycloastragenol in vivo and in vitro[D]. Beijing: Beijin g University of Chinese Medicine, 2013:34-35

[7] Jing ZHU, Stephanie LEE, Maurice K. C. HO, Yue qing HU, Hai hong PANG, Fanny C. F. IP, Allison C. CHIN, Calvin B. HARLEY, Nancy Y. I P, Yung H. WONG.In vitro Intestinal Absorption and First-pass Intestinal and Hepatic Metabolism of Cycloastragenol, a Potent Small Molecule Telomerase Activator[J]. Drug Metab Pharmacokinet.2010; 25(5): 477-86.