

Semi-Phyto Universal Solubilizer (SPUS) for enhancing solubility and bio availability of Bioactive compounds

Author: Velmurugan Shanmugham

Aqueous Solubility of Bio actives plays a significant role in Drug, Biopharma, Food, Dietary and Cosmetic formulations. Poor solubility is one of the biggest hurdles in developing these formulations as well as desired therapeutic effect. It is well proven that more aqueous soluble means rapid absorption which leads to more bioavailability in the body thereby decreases the dosage of Actives to a greater extent.

In food specifically the beverage industry suffers a lot with unavailability of Natural solubilizer. Moreover, the Cosmetic industry couldn't use some of the Phyto actives in their formulations due to non-aqueous solubility, even though they possess excellent biological activity.

What is AquaD?

AquaD is **Semi-Phyto Universal Solubilizer (SPUS)** and scientifically known as Diosgenin Polyethylene glycol succinate) is a water-soluble form of naturally occurring Diosgenin. Diosgenin, a steroidal sapogenin, occurs abundantly in plants such as *Dioscorea alata*, *Smilax China*, and *Trigonella foenum graecum*. This bioactive phytochemical not only is used as an important starting material for the preparation of several steroidal drugs in the pharmaceutical industry but has revealed also high potential and interest in the treatment of various types of disorders such as cancer, hypercholesterolemia, inflammation, and several types of infections. In fact, diosgenin has been described in the literature for its pharmacological potential, including the interesting underlying mechanisms of action, thereby confirming and extending the knowledge from its usage in traditional medicine. In this context, mainly over the past two decades, a series of preclinical and mechanistic studies have been performed to understand the real importance and benefits of diosgenin against a variety of pathologies including metabolic diseases (diabetes, obesity, and dyslipidemia, including hypercholesterolemia), inflammatory diseases, and cancer¹.

Aqua-D is produced by the esterification of Diosgenin succinate by polyethylene glycol 1000. In addition to serving as a water-soluble source of Diosgenin, Aqua-D is an amphiphilic compound with hydrophilic head and Lipophilic Tail. This dual combination of lipophilic and hydrophilic activities in a single molecule imparts unique properties. Aqua-D is a unique water soluble natural Diosgenin, used to enhance the bioavailability of Bio actives. It is a powerful emulsifier and solubilizer for fat soluble ingredients, as well as ingredients with poor solubility. Aqua-D is a miscible form of Diosgenin, is composed of a hydrophobic Diosgenin part and a hydrophilic PEG chain. It exhibits excellent drug delivery capability based on this special amphiphilic structure.

Physical and chemical properties of Aqua-D

Name	Diosgenin polyethylene glycol succinate
Appearance	Amber to pale yellow solid
Solubility	Soluble in Water, Acetone, Ethanol, Ethyl acetate, Isopropyl alcohol
Melting point	40 to 45°C
HLB value	~14.6
Decomposition temp	>200°C

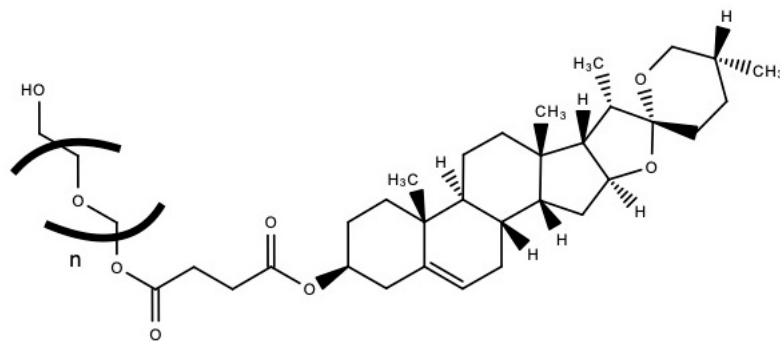


Figure 1. Chemical structure of Diosgenin Polyethylene Glycol succinate

Solubility enhancement

Curcumin, from the spice turmeric, exhibits anti-inflammatory, antioxidant, anticancer, antiviral, and neurotrophic activity and therefore holds promise as a therapeutic agent to prevent and treat several disorders. However, a major barrier to curcumin's clinical efficacy is its poor bioavailability. Efforts have therefore been dedicated to developing curcumin formulations with greater bioavailability and systemic tissue distribution².

Solubilizing capacity of AquaD-1000

Curcumin is formulated with Aqua-D Hot-melt process.



Figure 2: Curcumin Standard in Water



Figure 3: Curcumin formulated with Aqua-D in water (1% w/v aqueous solution of 30% w/w Curcumin)

Enhancing Bioavailability-Comparison of Release profile

Curcumin, a major active constituent found in *Curcuma* sp, is classified in group 4 of BCS (Biopharmaceutical Class System). This means solubility is a key factor when determining the absorption. In addition, low permeability is a second contribution for its low bioavailability after oral administration. According to Banrida et al., tested curcumin in CaCo2 cells indicated that curcumin is poorly permeable with a Papp (A → B) value of $2.93 \pm 0.94 \times 10^{-6}$ cm/s. Papp value in (B → A) study was found out to be $2.55 \pm 0.02 \times 10^{-6}$ cm/s, thus ruling out the role of efflux pathways in the low oral bioavailability of curcumin. In addition to poor solubility and permeability, the low bioavailability of curcumin is also worsened by intensive hepatic metabolism to more hydrophilic substances which are inactive.

In relation to that study, we also did an in vitro assay of challenging curcumin in liver homogenate and observed rapid degradation after incubation at 37 °C. Curcumin is reported as a potent anti-inflammatory agent; however, its complex problems led to clinical failure when this compound was used. BCS 4 drugs like curcumin are difficult to solve especially in the phase of formulation and delivery³.

Drug absorption following oral administration is dependent on release from the pharmaceutical formulation, dissolution in the physiological medium, and permeability across the gastrointestinal tract. Dissolution tests are an important tool for guiding the development of new formulations, manufacturing process evaluation, and assessment of lot-to-lot quality^{4,5}.

A collection of seven surfactants of various kinds were tested for their capability to release curcumin in pH 6.8 buffer. In a typical procedure, Curcumin is formulated with various surfactants by Solvent evaporation method. In this method, Curcumin 1g dissolved in 10ml of acetone and 3g of surfactants dissolved in 10ml of acetone separately. The Curcumin in acetone solution is added to the surfactant solution/suspension slowly under stirring. Finally, the acetone is removed under reduced pressure. The resultant mixture is encapsulated in “00” hard gelatin capsules. The dissolution and HPLC conditions are given below.

Dissolution condition		HPLC conditions	
Stirrer type	Basket	Column	ODS
Dissolution media	pH 6.8 phosphate buffer	Detection	420nm
Time	1hr	Flow rate	1ml per min
Stirrer RPM	100	Mobile phase	Mixture of citric acid in water (0.1%) and tetrahydrofuran (6:4)

Curcumin formulated with Aqua-D achieved highest release

From this dissolution experiment, Curcumin formulated with HPMC is having lowest release rate when compared to Curcumin formulated with Aqua-D. Curcumin formulated with PEG-1000 shows only 18.27% release of Curcumin when compared to Curcumin + Aqua D, the release is 80.37%. It is imperative that for an effective solubilizer and bioavailable enhancer a molecule should have both hydrophilic and lipophilic end. Most interestingly, Curcumin formulated with times E TPGS showed only 20.3% release which is 4.4 times lesser than Curcumin Aqua-D formulation. The Curcumin release and the Matrix details are illustrated as Figure 4 and Table 1 respectively.

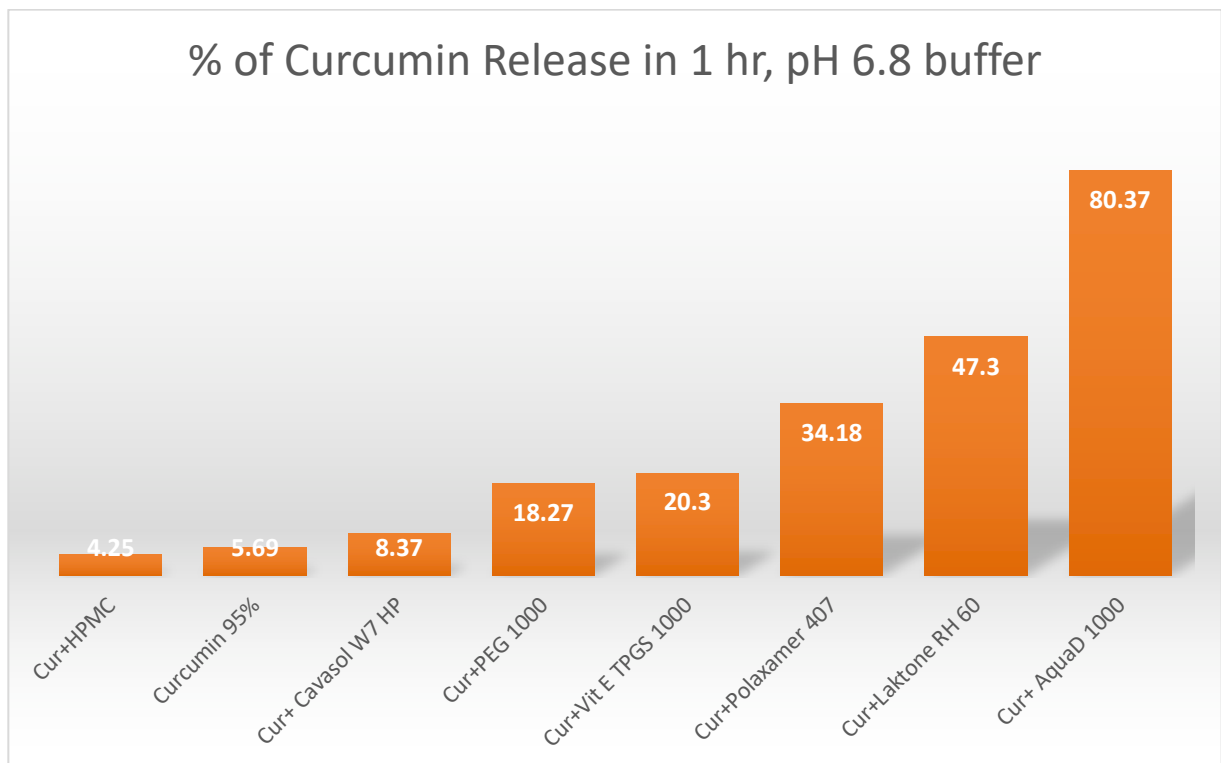


Figure 4: The highest release of Curcumin (80.37%) is observed in Curcumin + AquaD

Matrix	Curcumin Release	Solubilizer
Curcumin + HPMC	4.25%	Hydroxypropyl Methyl Cellulose
Curcumin 95%	5.69%	
Curcumin + Cavasol W7 HP	8.37%	hydroxypropyl-beta-cyclodextrin
Curcumin + PEG 1000	18.27%	Polyethylene glycol 1000
Curcumin + VIT E TPGS 1000	20.30%	Tocopherol Polyethylene glycol 1000
Curcumin + Polaxamer 407	34.18%	Polypropylene & Polyethylene glycol copolymer
Curcumin + Laktone RH 40	47.30	Hydrogenated Caster oil with PEG
Curcumin + Aqua-D	80.37%	Diosgenin Polyethylene Glycol Succinate

Table 1: Curcumin Matrix and Release details

AquaD solubilizes oils

In a laboratory experiment, Clove essential oil is formulated in the ratio of 1:3 with AquaD by hot melt procedure. In this the AquaD is melted at the temperature of 50°C with stirring and the Clove oil is slowly added under stirring. The resultant product is dissolved in water (1 :10 ratio). The olfactory analysis revealed that the aqueous solution is non-sticky.

AquaD formulatios with Phytochemicals

AquaD is formulated with several phytochemicals such as Forskolin from Coleus forskholii, Capsaicin from Capsicum annum, Azadirectin from Neem, 3-O-Acetyl-Beta boswellic acid from Boswellia and Azadirectin from Neem. The formulated product has greater aqueous solubility and also there is no sedimentation observed after 30 days.

AquaD™ can be used in various industries

- Finished formulation manufacturers like Capsule, Tablet, Oral syrups etc. to enhance the bioavailability.
- Beverage manufacturer to solubilize water insoluble actives.
- Biopharmaceutical as stabilizing agents.
- Dietary supplements/Functional Food manufacturer to solubilize and stabilize Phytochemicals.
- Cosmetics manufacture to solubilize water insoluble chemicals.

Applications of AquaD-1000

- 1. Solubilize Actives**
- 2. Prevent Actives from crystallization**
- 3. Protects Actives in the absorption process**
- 4. Enhance bioavailability of poorly absorbed actives**
- 5. Reduce drug toxicity or sensitivity on skin or tissues**
- 6. A vehicle in a semi-solid dosage form**
- 7. An emulsifier for injectable formulations**
- 8. A functional ingredient for inhalation dosage form**
- 9. A functional ingredient in self-emulsifying formulations**
- 10. A thermal binder in melt granulation/extrusion process**

Note: Aqua-D is suitable for Hot-Melt extrusion, Spray drying and Solvent evaporation processes

AquaD is recognized by Scientist and Industrialists

Best Innovative product of the year (2019-20) awarded by Karnataka Innovation & Technology society (Government of Karnataka, India). The award was finalized by a 15-member panel consists of Eminent scientists, Professors and industrialists.

Conclusion

Worldwide the researchers and Formulators are looking for Naturally derived effective solubilizer and The solubilizers available in the markets are chemically derived. AquaD is a Semi-phyto natural solubilizer and it can act as universal solubilizer. It almost compatible with all kind of materials such as Pharma, Chemicals, Oils, Biopharmaceutials etc.

Contact:

Phytosol India Pvt Ltd
#1368, II Main, II Cross, Samrat Layout
Arekere, Bangalore. 560 076
Mob: 9972891187 &9945081007
Email: phytosolindia@gmail.com

Note: AquaD is a Patent pending & Application No. 202041016518.

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