AquaSolve™ Hypromellose Acetate Succinate (HPMCAS)

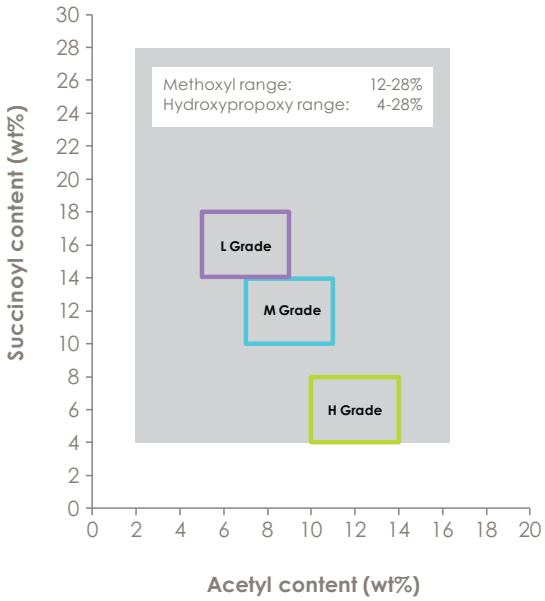
Versatile pharmaceutical polymers for improved solubility

AquaSolve HPMCAS is a mixture of acetic acid and monosuccinic acid esters of hydroxypropylmethyl-cellulose. AquaSolve HPMCAS is used as a solid dispersion polymer for bioavailability enhancement of poorly soluble active pharmaceutical ingredients (APIs). The versatility of this polymer in addressing solubility issues is a result of its unique properties. These properties lead to enhanced absorption when HPMCAS-based solid dispersions are dosed orally.

Features and benefits of AquaSolve HPMCAS

Feature	Benefit
Several substitution ranges	Scope for API-dependent formulation flexibility
Low solution viscosity in multiple organic solvents	Economical and controllable spray-dried dispersion processes
High Tg	Excellent physical stability due to low drug mobility
Performance matches monograph-compliant competitive products	Reduced risk in excipient sourcing and ease of interchangeability
HPMCAS is amphiphilic	Insoluble drug molecules interact with the hydrophobic regions; hydrophilic regions allow the formation of colloids in aqueous solution
Enteric polymer, so partially ionized above pH 5	Charge on the polymer minimizes the formation of large agglomerates, thus stabilizing drug-polymer colloids

AquaSolve HPMCAS is also used as an enteric coating polymer and in preparation of sustained drug-release formulations; the release rate of the API from the matrix is pH dependent.



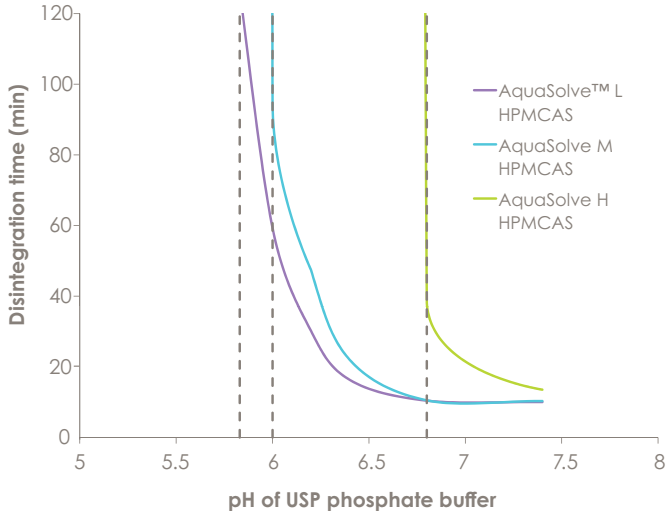
AquaSolve HPMCAS is available in three grades differentiated by degree/ratio of substitution. Each grade is available in two particle sizes. Consult the product data sheet or the excipient information package for further details on specifications. Additional substitution levels and ranges are available upon request. Detailed product information is available in the *AquaSolve™ Hydroxypropylmethylcellulose Acetate Succinate Physical and Chemical Properties Handbook*.

AquaSolve HPMCAS complies with National Formulary and Japanese Pharmaceutical Excipients specifications (shaded box)

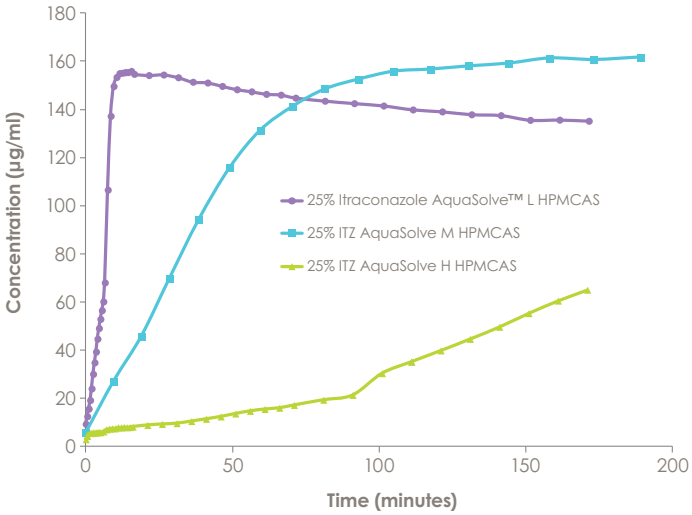
Improved solubility can be polymer dependent

Improved solubility and bioavailabilty of an API is dependent upon which grade of polymer is selected as well as upon the API. The properties of three APIs we have worked with are shown in the table.

Property	Itraconazole	Ezetimibe	Felodipine
Tm (°C)	166.2	163	141.6
Tg (°C)	59	70	43
LogP	5.66	4.5	4.83
pKa1	3.70 (weak base)	9 (weak acid)	Neutral
Solubility (mg/l)	<1	8	19.7

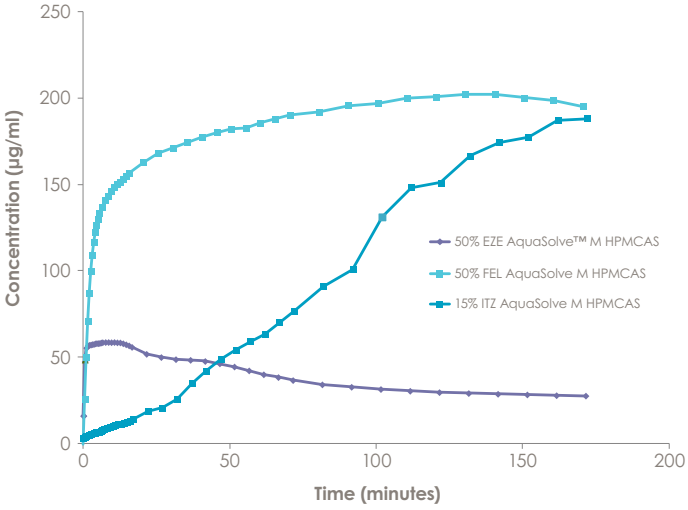


The H grade of AquaSolve HPMCAS dissolves at a higher pH than the L and M grades and so it takes longer to release in gastric fluid.



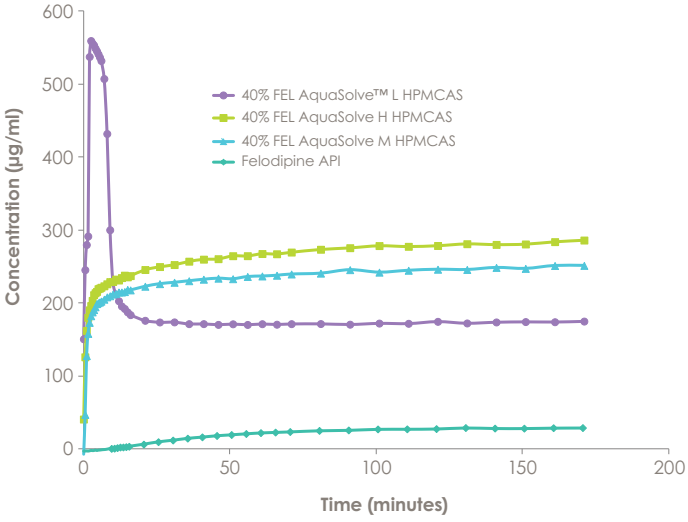
Itraconazole is a weak base and lipophilic, hence a more hydrophilic grade of HPMCAS (indicated by a higher succinoyl ratio) is required for rapid dissolution.

Improved solubility can be API dependent

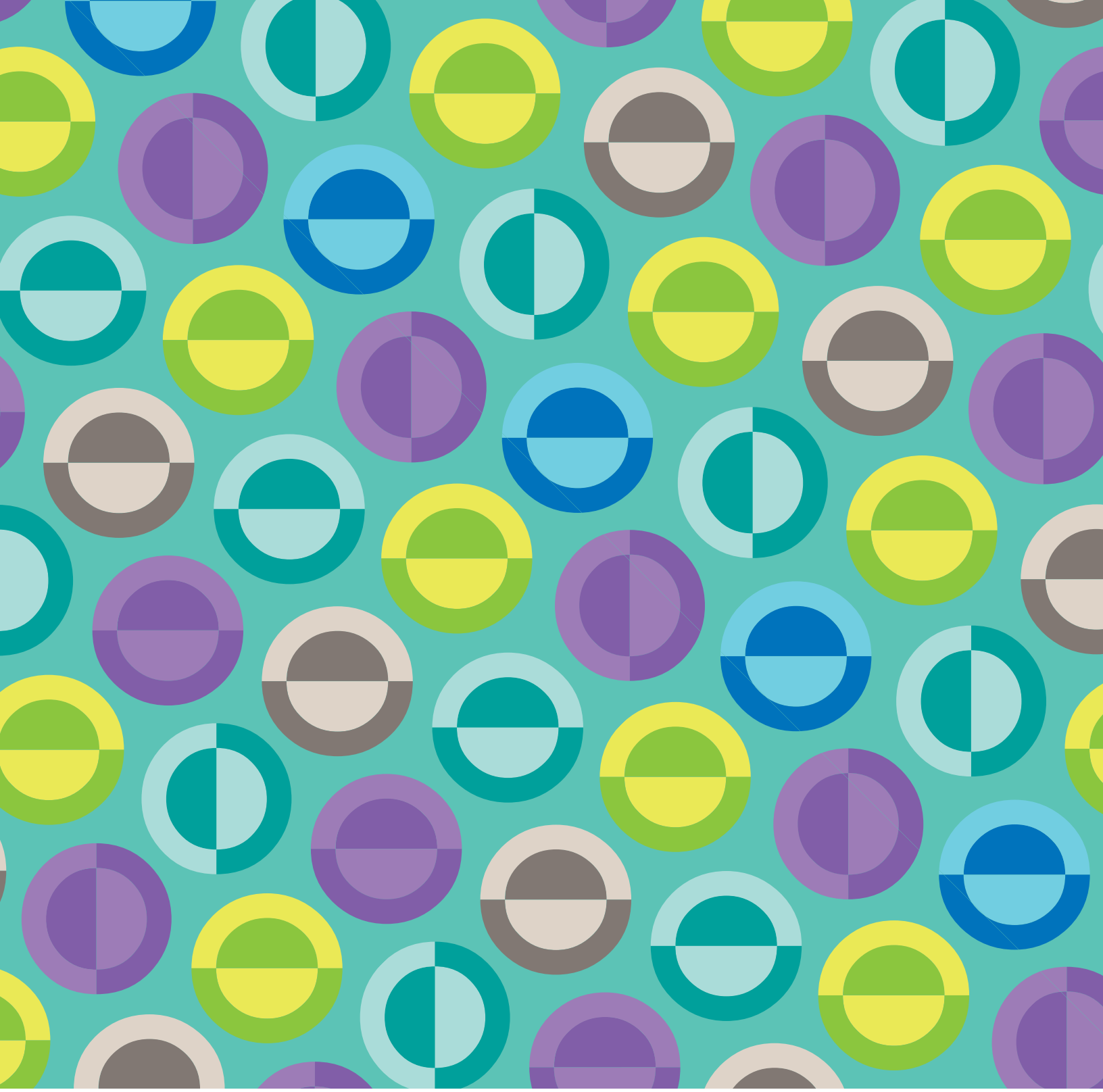


Differences in solubility across APIs can be observed when using the same grade of HPMCAS with different APIs as can be seen in the variation in solubility for solid dispersions of ezetimibe, felodipine and itraconazole made with M grades of AquaSolve HPMCAS. The release profiles of the three APIs vary widely with the same (M) grade of HPMCAS.

Delayed recrystallization



There have been a number of reports demonstrating superior performance of HPMCAS over existing polymers in terms of solubilizing efficacy in vivo and recrystallization inhibition during storage. Some HPMCAS solid dispersions exhibit characteristic spring-and-parachute shape dissolution curves, whereby a large percentage of API can be released quickly and supersaturation can be maintained for prolonged time periods. Each grade of AquaSolve HPMCAS maintains a high concentration of felodipine in solution over time, but the M and H grade curves demonstrate this prolonged supersaturation particularly well.



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