Formulation of Extended Release Vitamin C Supplements

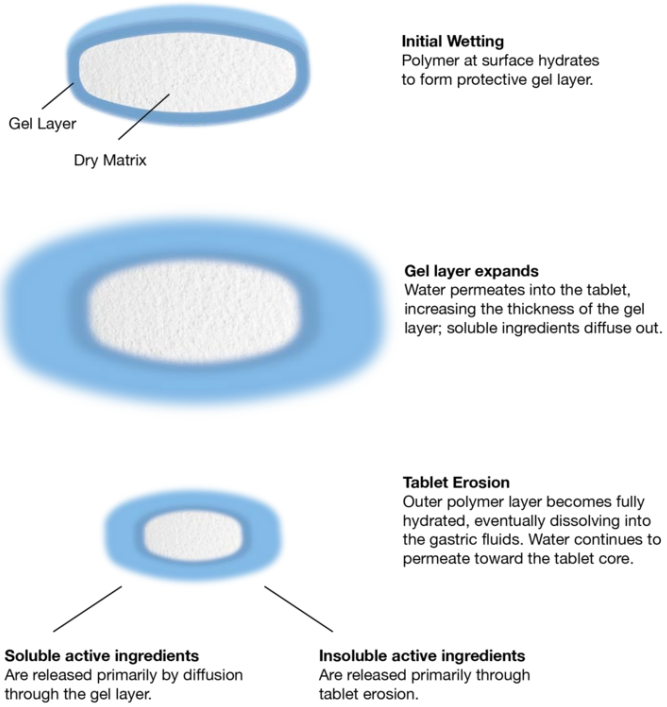
Dietary supplements are widely used to add health-promoting nutrients to an individual's diet for the prevention and treatment of nutrient deficiencies[1] and support a healthy lifestyle. Controlled release tablets are formulated to make the active ingredient available to the body over an extended period following ingestion. This typically enables a once-a-day routine which promotes adherence as the number of tablets consumers need to take is decreased.

Vitamin C, or ascorbic acid, is a water-soluble vitamin and is widely taken as an oral supplement as it is not well stored in the body. As well as being a nutrient the body needs to form blood vessels, cartilage, muscle, and collagen in bones, it is an antioxidant that helps protect against the effects of free radicals and helps the body absorb and store iron. Single doses of vitamin C greater than 200 mg have lower relative bioavailability and taking several smaller doses throughout the day may be more effective than a single large dose. However, taking multiple tablets throughout the day is not consumer friendly. An extended release formulation solves this problem with a single dose that releases vitamin C more slowly, providing improved bioavailability.

This case study demonstrates the formulation development of an extended release tablet dosage form using METHOCEL™ Premium Cellulose Ethers as the rate-controlling polymer.

Matrix systems, for extended release, are popular because they are well understood and can be manufactured with conventional equipment and processes and have broad regulatory acceptance. In addition, consistent control of drug release has been successfully demonstrated in marketed products containing high and low drug doses. The use of METHOCEL™ in hydrophilic matrix tablets means the release of active ingredients can be fine-tuned for high or low solubility materials.

Mode of Action for Extended Release Matrix Tablets



Case Study – Vitamin C Extended Release Formulation

Due to the high solubility of vitamin C, the first recommendation for dietary supplements is to use a high viscosity grade of METHOCEL™ premium cellulose ethers. Hypromellose polymers (METHOCEL™) are derived from cellulose with the length of the cellulose molecule determining the molecular weight, viscosity, gel strength and drug release. Higher viscosity results in slower release rates, depending on the level of use. In this study, three different viscosity grades (K4M, K15M, and K100M) were evaluated at different inclusion levels (5%, 10% and 15 % w/w) to evaluate the impact on the release rate for a 500 mg dose of vitamin C.

Tablets compressed on a rotary tablet press were round-shaped, standard concave, 12.7 mm (0.5-inch) in diameter with a target tablet weight of 770mg for a 500 mg dose (65%) of the active ingredient (Table 1). The target compression force for all tablets and formulations was 20, 25, and 30 kN with increased tablet hardness observed with increasing compression force within a range of 8.4-13.8kp.

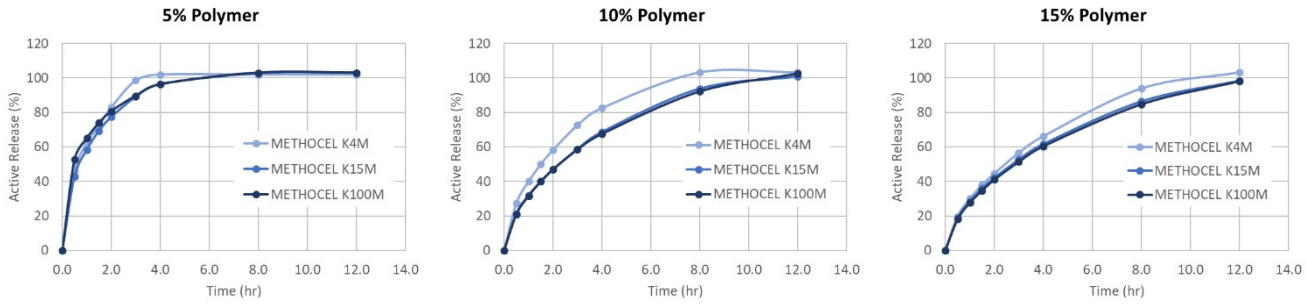
Table 1: Tablet Core Formulation

Cure Tablet Ingredients	mg/tablet	% w/w
Vitamin C	**500.5**	**65.0**
METHOCEL K4M, K15M, K100M	**38.50 to 115.50**	**5.0 to 15.0**
Microcrystalline cellulose (MCC) 90M	**225.225 to 148.225**	**19.25 to 29.25**
Colloidal silicon dioxide	**3.850**	**0.50**
Magnesium stearate	**1.925**	**0.25**
Total Tablet Weight	**770.0**	**100.0**

Results

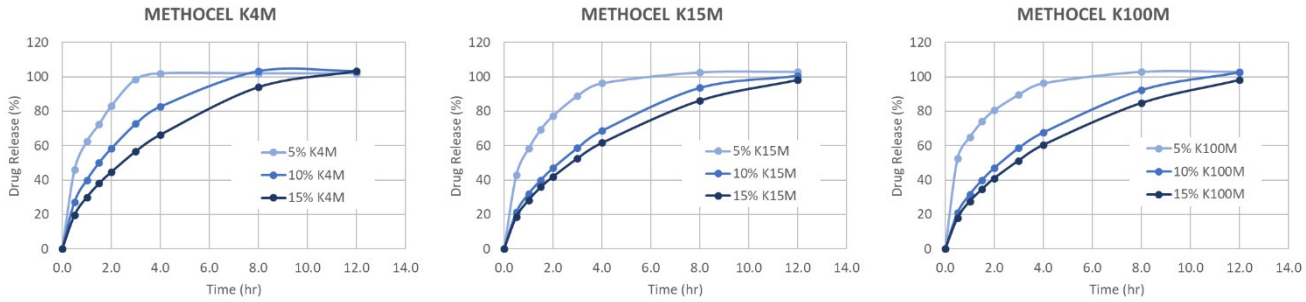
Due to the relatively low level included in the formulation for the different viscosity grades of METHOCEL™, there was no significant impact on the release profile (Figure 1). With low polymer levels, a robust gel layer may not exist to adequately control release. Therefore, properties such as the solubility of the active ingredient (vitamin C) and diluent selection influence the release mechanism to a greater degree. It is expected that when higher polymer levels are used then a difference in release performance will be seen between viscosity grades.

Figure 1: Effect of Polymer Grade on Release of Vitamin C



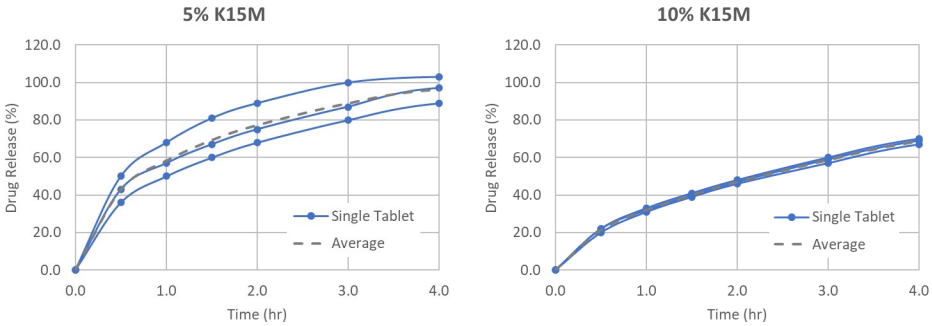
Although the viscosity grade did not have a significant effect on release profile the use level did, with higher inclusion levels resulting in slower release profiles (Figure 2).

Figure 2: Effect of Polymer Concentration (%) on Release Rate of Vitamin C



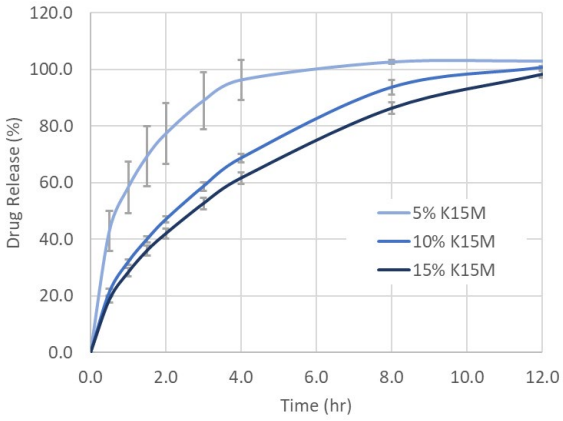
Low levels of controlled release polymer may result in tablet-to-tablet performance variability. Increasing the level of K15M polymer concentration from 5% to 10% for this formulation eliminates the tablet-to-tablet variability (Figure 3).

Figure 3: Comparison of METHOCEL™ K15M Inclusion Levels on Release Performance



The reduction of performance variability is observed at increasing polymer levels from 5%, 10% and 15% in the formulation (Figure 4). Tablet-to-tablet dissolution performance variability is highest at the 5% K15M inclusion level, as seen in large error bars. Performance variability decreases with the 10% and 15% inclusion levels.

Figure 4: Performance Variability Reduces as Polymer Level Increases



The practice of using a lower than recommended polymer level in a matrix tablet formulation may impact performance variability (dissolution).

To overcome performance variability, the recommendation is to:

- Select tablet diluents that add formulation flexibility and performance
- Select a METHOCEL™ molecular weight grade and inclusion level based on the target release profile and performance
- Consider the use of METHOCEL™ CR grade to reduce/eliminate release variability

Conclusion

Extended release matrix tablets can be utilized to prolong the release rate for vitamin C, overcoming the need for multiple daily doses.
Modified Release technologies offer a safe, reliable delivery system for differentiated dietary supplements that are consumer friendly.

References

1. Healthline. (2019). Nutritional Deficiencies (Malnutrition). https://www.healthline.com/health/malnutrition

For more information, contact your Colorcon representative or call:

North America	Europe/Middle East/Africa	Latin America	India	China
+1-215-699-7733	**+44-(0)-1322-293000**	**+54-1-5556-7700**	**+91-832-6727373**	**+86-21-61982300**

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