Capsugel®

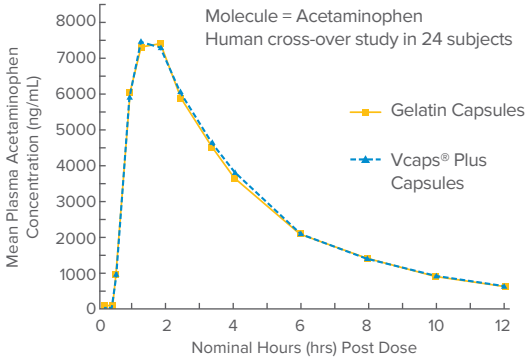
Vcaps® Plus Capsules: The new standard in HPMC capsules—

Immediate release *in-vivo* performance bioequivalent to gelatin and consistent dissolution across changing pH and ionic strength.

Vcaps Plus capsules can optimize capsule disintegration for pharmaceutical products with the ability to release contents independent of pH and ionic strength of the test media. Made through a newly developed thermo-gelation process, the capsule avoids the addition of gelling systems that can react to the pH or ionic strengths of dissolution media. And a new *in-vivo* study demonstrates that Vcaps Plus capsules are equivalent to gelatin in terms of human pharmacokinetics profile.

Finally, a superior specialty polymer capsule with proven gelatin-like performance without cross-linking potential, Vcaps Plus is the new capsule standard with benefits of narrow weight variability, impressive resistance to heat and humidity, and validated manufacturing experience. By reducing variability, Vcaps Plus capsules are quickly becoming a powerful new tool to reduce timelines in drug product development.

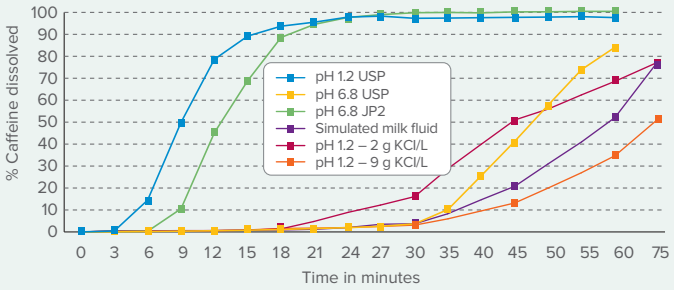
Proven Bioequivalence to Gelatin



Mean *in-vivo* acetaminophen plasma concentration profiles over 12 hours

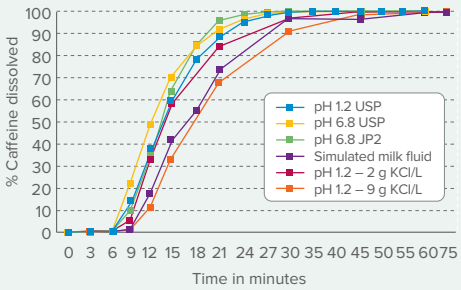
Secondary gelling systems create variability while Vcaps Plus capsules, without gelling agents, provide ionic and pH independence in dissolution.

Influence of gelling systems on HPMC capsules in dissolution testing



In-vitro dissolution of caffeine filled in hypromellose capsules produced with gelling systems

In-vitro dissolution of caffeine in Vcaps Plus® capsules



Caffeine *in-vitro* dissolution with various dissolution media exhibit pH independence with Vcaps® Plus capsules

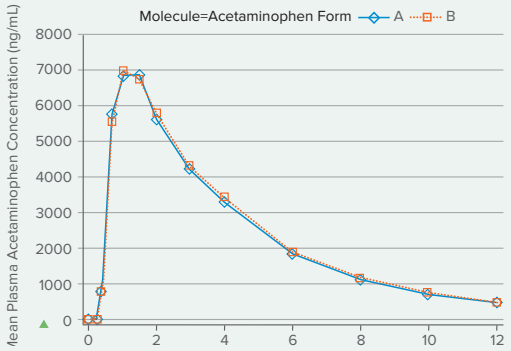
In-Vivo performance demonstrates Vcaps Plus bioequivalence to gelatin.

To study the performance of Vcaps Plus with different types of compounds and to understand the *in-vivo* performance, a bioequivalence study was performed as a single-center, open label, single dose randomized 2-way crossover study with 24 male subjects under fasted conditions.

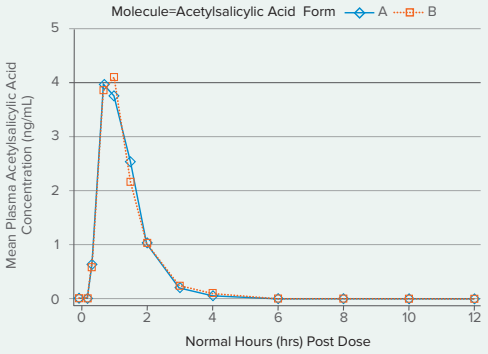
The study used Excedrin Extra Strength caplets as a sensitive marker for *in-vivo* dissolution and absorption of caffeine (65 mg), acetylsalicylic acid (250 mg) and acetaminophen (250 mg). The caplets were filled into gelatin or Vcaps Plus size 00 capsules.

Results for the acetaminophen, acetylsalicylic acid and caffeine PK parameters are shown at the right at the top of each graph of the main plasma concentration over time for each ingredient. **The results are nearly identical for the mean plasma concentration levels for all three ingredients.**

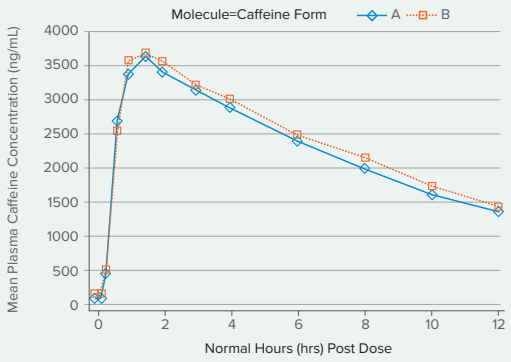
(a) Mean *in-vivo* acetaminophen plasma concentration released over 12 hours.



(b) Mean *in-vivo* acetylsalicylic acid plasma concentration released over 12 hours.



(c) Mean *in-vivo* caffeine plasma concentration released over 12 hours.



Designed To Improve Product Stability

Temperature stability. Internal studies showed no changes in color, transparency, loss on drying (LOD), disintegration, dissolution or filling performance at low temperatures, and no changes in disintegration, dissolution or mechanical performance at high temperatures.

Long-term storage stability. An internal study showed no change in physical performance over extended exposure to a range of storage temperatures and relative humidity.

Effects of moisture. Study results indicate that as a consequence of being less hygroscopic, moisture transfer from a Vcaps Plus capsule to the encapsulated product could potentially be reduced, helping to maintain product stability. Also, since water does not act as a plasticizer for Vcaps Plus, the capsules are less likely to break even in dry conditions, helping to maintain stability of products inside the capsule.

Made To Reduce Development Timelines

Capsule filling machine performance. Performance trials on many common high-speed capsule filling machines indicate that Vcaps Plus capsules, with their smooth and shiny finish, show better performance than HPMC capsules containing gelling agents, in terms of filling and rejection rate, and have a similar performance to gelatin capsules.

Regulatory acceptance. All primary components of Vcaps Plus capsules are acceptable for use in pharmaceutical and dietary supplement oral dosage applications in the US, Canada, EU, Japan and Australia. In addition, Vcaps Plus capsules are certified Kosher by Ko, approved for vegetarians by the Vegetarian Society and Halal by IFANCA.

Learn more about the new *in-vivo* results comparing Vcaps Plus HPMC Capsules and gelatin capsules, which demonstrate the bioequivalency of HPMC in multiple dissolution profiles.

Capsugel®

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