Enhanced Stability of Folic Acid by Encapsulation in Ph-Responsive Gated Mesoporous Silica Particles

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Extended Abstract

Folic acid (FA), a water-soluble B vitamin, is essential to numerous bodily functions, and indispensable in cases of pregnancy (Lucock, 2000). FA is sensitive to physical factors such as low pH, temperature, pressure, and light (Nguyen *et al.*, 2003; Yakubu & Muazu, 2010). Thus, food naturally occurring folates are affected during food processing or digestion provoking FA deficiencies. Moreover, most of the FA supplements fail due to insufficient release of the vitamin (Giebe & Counts, 2000). As a consequence, the encapsulation of FA to achieve both, prevention of environmental degradation and controlled release along the digestive tract, is a promising strategy.

In recent years, mesoporous silica particles (MSPs) have been proposed as perfect candidates for controlled release systems due to their high stability, large loading capacity, high surface and biocompatibility (Slowing *et al.*, 2008; Pérez-Esteve *et al.*, 2015). Despite its extensive use, little works studying the influence of MSPs to protect labile bioactive molecules from physical and chemical degradation are available.

The objective of this work was to study the influence of FA encapsulation in MSPs on its stability enhancement against pH, light and temperature exposure. To this, MCM-41 microparticles were loaded with FA and functionalized with amines acting as pH-dependant molecular gates. Then the stability of entrapped FA, in comparison with the free form, was studied.

Results showed total degradation of free FA by light exposure, whereas the MSPs stabilized considerably the entrapped vitamin. The stability of free and entrapped FA was similar after temperature treatment and no significant differences were detected. Moreover, FA release was triggered at pH 7.5 which simulated intestine conditions where absorption of the vitamin takes place. In contrast at acidic pH 2.0, the gates were closed and the vitamin was protected in acidic surrounding, mimicking the human stomach. As a conclusion, the encapsulation of the vitamin in MSPs makes it a perfect candidate for an alternative supplement which could be introduced into food systems to enhance its stability and bioavailability.

Giebe, K., & Counts, C. (2000). Comparison Of Prenate Advance With Other Prescription Prenatal Vitamins: A Folic Acid Dissolution Study. *Advances in Therapy*, 17(4), 179–183.

Lucock, M. (2000). Folic Acid: Nutritional Biochemistry, Molecular Biology, And Role In Disease Processes. *Molecular Genetics and Metabolism*, 71(1-2), 121–138.

- Nguyen, M.T., Oey, I., Verlinde, P., van Loey, A., & Hendrickx, M. (2003). Model Studies On The Stability Of Folic Acid And 5-Methyltetrahydrofolic Acid Degradation During Thermal Treatment In Combination With High Hydrostatic Pressure. *Journal of Agricultural and Food Chemistry*, 51(11), 3352–3357.
- Pérez-Esteve, E., Fuentes, A., Coll, C., Acosta, C., Bernardos, A., Marcos, M.D., Martínez-Máñez, R., & Barat, J.M. (2015). Modulation Of Folic Acid Bioaccesibility By Encapsulation In Ph-Responsive Gated Mesoporous Silica Particles. *Microporous and Mesoporous Materials*, 202, 124-132.
- Slowing, I.I., Vivero-Escoto, J.L., Wu, C.W., & Lin, V.S.Y. (2008). Mesoporous Silica Nanoparticles As Controlled Release Drug Delivery And Gene Transfection Carriers. Advanced Drug Delivery Reviews, 60, 1278-1288.
- Yakubu, S., & Muazu, J. (2010). Effects Of Variables On Degradation Of Folic Acid. Der Pharmacia Sinica, 1(3), 55–58.