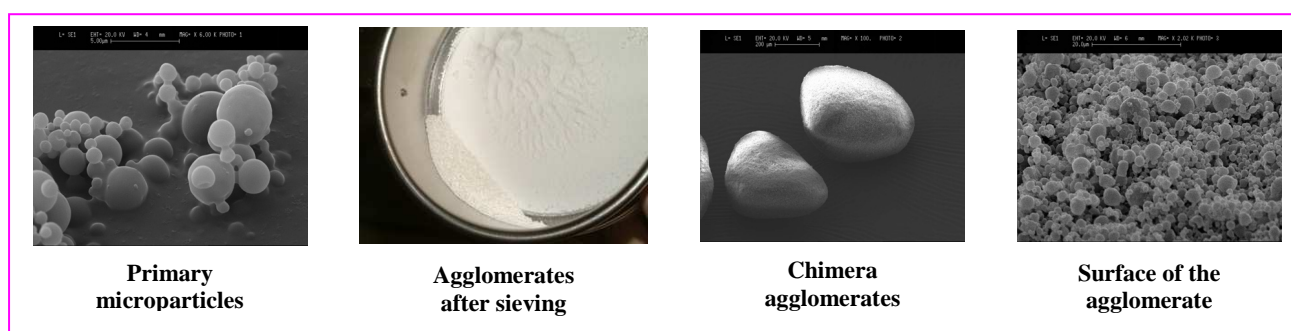


## Chimera agglomerates for buccal or oral immediate release of levothyroxine

Dott. Gaia Colombo – University of Ferrara – Consorzio TEFARCO Innova

Thyroxine buccal administration aims to innovate the chronic treatment of thyroidal pathologies. Deposited into the mouth, this prompt release formulation is designed to promote drug absorption mainly across the oral mucosa. Hence, a more reproducible absorption could be attained. The system consists in primary thyroxine-containing microparticles agglomerated to obtain a free flowing powder. The system's chimerical structure temporarily masks the microparticles until their release in the aqueous oral cavity.



### 1. Description of the product

Chimera agglomerates are clusters of smaller particles held together by weak bonds and obtained by rolling or sieving primary drug microparticles. Owing to their flow properties, they are easier to administer compared to microparticles.

These soft structures are suitable for drug administration directly into the oral cavity as they rapidly disaggregate in presence of the mucosal fluid, providing prompt drug release for absorption.

Moreover, the high dissolution rate makes them similar to an extemporaneous liquid formula, useful for immediate drug release in the GI tract, especially for drugs unstable in solution.

Thus, this dosage form could improve the therapy with drugs such the thyroid hormone (thyroxine), having critical oral bioavailability.

### 2. Innovative aspect of the product

The therapy with thyroxine is the only approach to treat hypothyroidism. In most cases, thyroxine is chronically administered per os lifetime. Since this approach has revealed serious bioavailability issues (high variability in drug gastrointestinal absorption), the interest in new dosage forms providing proper drug release and absorption is high.

Buccal administration of chimera agglomerates prepared from microparticles containing thyroxine with suitable excipients, can innovate the conventional therapy with the hormone. The peculiar features of this dosage form lie in the velocity by which the agglomerates reconstitute the primary microparticles immediately after administration. Once released in the oral cavity, the drug comes in contact with the mucosa (permeable and vascularized) and can be rapidly absorbed into the blood.

The project of using chimera agglomerates applies to pharmaceutical industries interested in innovating the therapy with thyroxine. In addition, the need of designing new devices for accurate administration (i.e., control of the amount of agglomerates deposited in the mouth) is also relevant in the development of this product.

### 3. Main advantages of the offer

In the case of thyroxine, a drug that is active at very low doses, the project of using chimera agglomerates could increase the drug bioavailability without a drastic change of the administration route. In fact, all drug not absorbed from the oral cavity, would be swallowed and eventually absorbed from the intestine. In addition, since liquid formulations of thyroxine are also available that are characterized by poor chemical stability, these chimera agglomerates easy to disperse in a liquid would be useful to produce an extemporaneous dosage form.

### 4. Technology key words

Hypothyroidism, levothyroxine, chimera agglomerates, buccal

### 5. Current Stage of Development

Work in progress – Tested in laboratory

### 6. Intellectual Property Rights

The product is covered by patent and available for licensing.

### Technical and scientific publications

Russo P., Colombo P., Bettini R., Sonvico F. and Buttini F. In Proceedings of Respiratory Drug Delivery IX 2004. Palm Desert, CA (USA), 2004.

Russo P., Buttini F., Sonvico F., Bettini R., Massimo G., Sacchetti C., Colombo P., Santi P. Chimeral agglomerates of microparticles for the administration of caffeine nasal powders. J. Drug Del. Sci. Tech (2004) 14(6) 449-454.

Russo P., et al., 'Primary Microparticles and Agglomerates of Morphine for Nasal Insufflation', J. Pharm. Sci. 2006, 95, 12, 2553-61.

G. Colombo, P. Russo, F. Sonvico, E. Hesse, A Dal Piaz, L. Ferraro, F. Bortolotti, In vitro and in vivo study of a desmopressin nasal powder,. In Proceedings of Respiratory Drug Delivery Europe 2007, Paris (F), 2007, pp. 345-348.

Soft agglomerates containing microencapsulated levothyroxine for buccal or oral delivery, G. Colombo, F. Bortolotti, P. Colombo, E. Menegatti, F. Sonvico, 16<sup>th</sup> International Symposium on Microencapsulation, Lexington KY (USA), Sept.. 9-12<sup>th</sup>, 2007.

"Compositions in powder form made of soft agglomerates of a micronized drug and of a two-components excipient, and process for their preparation", Raffin R., Colombo P., Sonvico F., Colombo G., Rossi A., Buttini F., PCT/EP2007/061559, 26/10/2007

Soft Agglomerates of Pantoprazole Gastro-resistant Microparticles for Oral Administration and Intestinal Release, RP. Raffin P. Colombo, F. Sonvico, FS. Polleto, G. Colombo, A. Rossi, AR. Pohlmann, SS. Guterres. J. Drug Deliv. Sci. Tech. 2007, 17(6): 407-413.

### CONTACT

info@biopharmanet.eu

Tel.: +39 0521 905073 Fax: +39 0521 905006