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Orally administered phenylalanine ammonia lyase microcapsules for the management of phenylketonuria (PKU)

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Unmet Need

Phenylketonuria (PKU) is an inherited disorder that increases levels of phenylalanine in blood. Phenylalanine is an amino acid obtained through diet and found in all proteins and in some artificial sweeteners. If PKU is not treated, phenylalanine can build up to harmful levels in the body, causing intellectual disability and other serious health problems. Occurrence varies among ethnic groups and geographic regions worldwide. In the US, PKU occurs in 1 in 10,000 to 15,000 newborns.

Currently the primary treatment for phenylketonuria includes:

- A lifetime diet with very limited intake of protein-rich foods containing phenylalanine
- A PKU (nutraceutical) formula to provide sufficient essential protein (without phenylalanine) and nutrients crucial for growth and general health.

Opportunity

Replacing the rigorous diet, orally administered microcapsules serve as miniature factories for rapid and selective removal of phenyalanine from diet. Not intended for oral absorption, they will eventually be eliminated in the feces.

- Microcapsules are non-digestible and will maintain structural integrity during their transit through the gastrointestinal tract.
- Phenylalanine in solution diffuses into the microcapsules and is rapidly metabolized to trans cinnamic acid by the encapsulated phenylalanine ammonia lyase.
- Microcapsules administered along with food will selectively metabolize phenyalanine from diet and consequently reduce its absorption. Oral administration of phenyalanine ammonia lyase microcapsules to phenyketonuric patients will allow patients to consume a relatively normal diet and yet accrue therapeutic benefits from the markedly decreased absorption of phenylalanine. It will free phenyketonuric patients from the onerous constraints of lifelong compliance with a synthetic, poorly palatable diet.
- Microcapsules encapsulating a functional enzyme represents a “platform technology” for the selective removal of specific nutrient from diet. The platform technology can be used to manufacture microcapsules that encapsulate enzymes involved in drug metabolism, which can then be administered orally along with drugs to enhance drug exposure.

Unique Attributes

- Microcapsules in the low micron size present a large surface area for rapid metabolism of phenylalanine.
- The core of the microcapsules is formulated with coencapsulants and presents a nurturing microenvironment to maximize the activity of encapsulated phenylalanine ammonia lyase.
- The semi-permeable membrane does not permit larger molecular weight gastrointestinal proteases to diffuse into the microcapsules. In addition,
  - The membrane does not allow the very large molecular weight phenylalanine ammonia lyase to diffuse out of the microcapsules.
  - The microcapsules can protect the encapsulated phenylalanine ammonia lyase from proteolytic degradation in the gastrointestinal tract.

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Stage of Development Preclinical Studies

Intellectual Property Provisional patent in force. PCT filed April, 2017.

Collaboration Opportunity Actively seeking licensee for commercialization or collaboration to complete preclinical studies.

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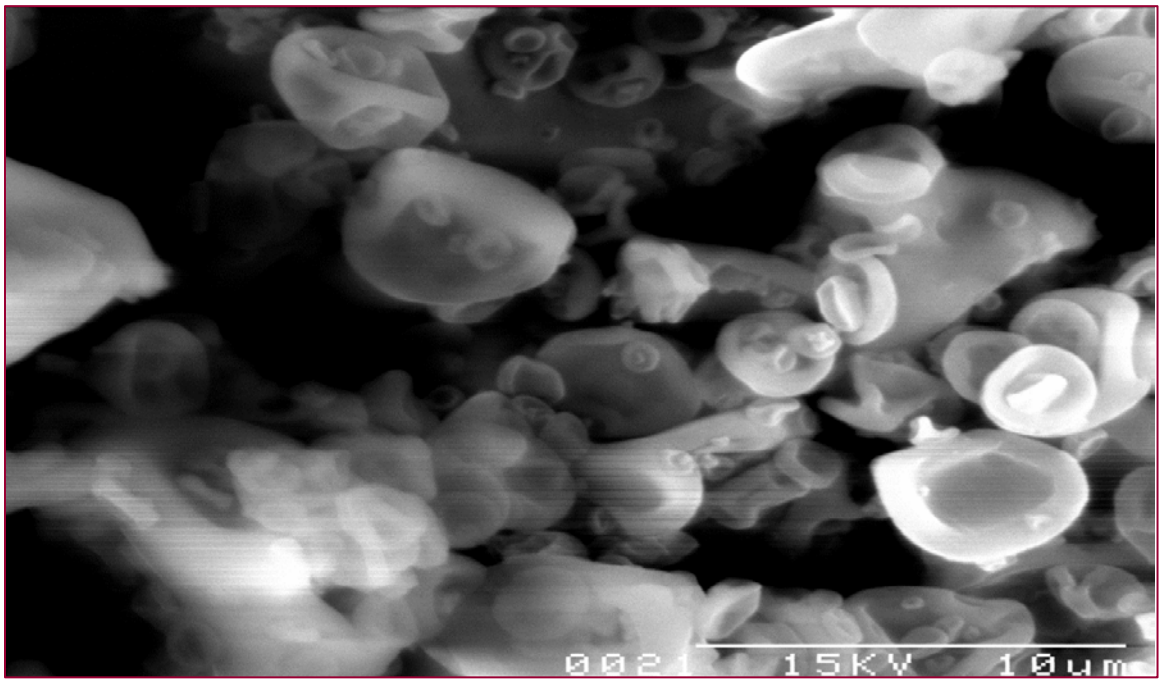

Scanning electron micrograph of spray dried microcapsules