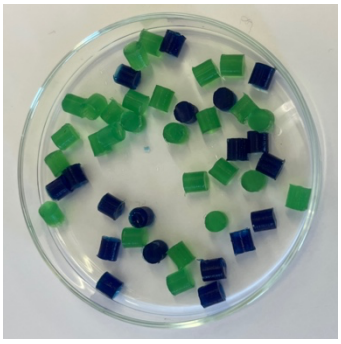
Technology Offer

# HaPILLness: Semi-Solid Formulation for Voluntary Oral Administration of Bioactive Compounds to Rodents

**KEYWORDS:** Biomedical Sciences; Pharmacology and Toxicology; Pre-Clinical Assays; Voluntary Oral Drug Administration; Rodents; Semi-Solid Matrix; Jelly; Stress-Free; Non-Invasive; Metabolic Homeostasis Preservation.

Oral administration of bioactive compounds to animals is frequently associated with great difficulties due to the reluctance of the animals to ingest tablets, pills or medicated feed, especially if these substances have an unpleasant taste. During compound screening and drug development, chronic oral drug administration to laboratory rodents is often required and non-invasive methods providing voluntary acceptance are warranted. Likewise, toxicants formulations to control rodent's activities around dwellings (and their unquestionable impact on public health) are currently incorporated into baits containing attractants (e.g. grains, fats, seeds, flavor enhancers) to avoid trap shyness and increase rodenticide's voluntary consumption and effectiveness.



The present invention provides an innovative technological solution to leverage the 3Rs principles towards a more humane alternative of rodents' precise oral drug dosing. The delivery formula claimed herein mimic the pill dosage form widely used in human clinical practice. It comprises non-toxic, food acceptable and inert excipients, providing a semi-solid texture suitable to uniformly incorporate bioactive compounds (e.g. drugs, vegetable biomasses, toxins) that are readily accepted by rodents (full consumption < ≈ 5 minutes) in both healthy and diseased conditions (e.g. CNS impairments), with superior therapeutic/toxicologic compliance. These new oral matrices are easy to manufacture and accomplish a new oral drug dosing refinement method easing the harm-benefit dilemma put forth by animal research, by both effectively reducing animal discomfort and pain and improving reliability of results, by reducing stress' impact on pathophysiology and consequent variability of scientific data.

| ADVANTAGES | APPLICATIONS |
|---|---|
| • Allows for individual precise dosing (amount of drug/body weight).<br>• Requires small amounts of drug (when compared to drugs admixed in the food or drinking water).<br>• Overcomes drug hydrophilicity/lipophilicity requirements for vehicle-solubilization.<br>• Does not elicit significant stress responses.<br>• Is efficient for repetitive and long-term delivery of bioactive compounds into rodents.<br>• Be a carrier of bioactive compounds to rodents.<br>• Achieve high acceptance index and voluntary oral consumption in a reproducible fashion.<br>• Preserve metabolic profile and welfare of experimental laboratory rodents. | • Oral administration of drugs and bioactive compounds to rodents.<br>• Production of toxicant baits for rodents. |

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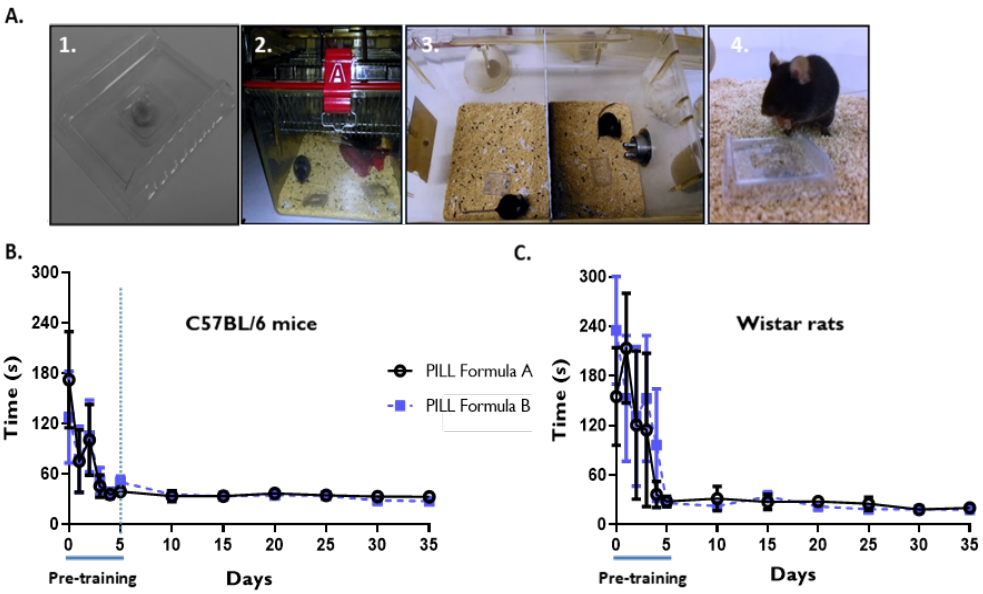


**A. Representative images of our PILL following manufacture, PILL administration protocol and experimental settings:** 1. Representative image of PILL shape and size; 2. Representative image of healthy C57BL/6 mice in cage with environmental enrichment; 3. The protocol for our PILL administration set up, where animals are pair-housed and a partition is inserted ONLY for the duration of consumption [optimal voluntary acceptance occur < 5 minutes]; 4. Representative image of animal's voluntarily consuming our PILL.

**B. Graphic depicting the evolution of time healthy C57BL/6 mice** spent to consume PILL Formula A and B following the first exposure in day 1 until day 5 (pre-training, 3-5 day period where animals experience mild fasting to overcome their innate neophobia) and over a period of 30 consecutive days of daily vehicle consumption (n= 6-8 experimental group). Data are presented as mean ± SEM.

**C. Graphic depicting the evolution of time healthy Wistar rats** spent to consume PILL Formula A and B following the first exposure in day 1 until day 5 (pre-training, 3-5 day period where animals experience mild fasting to overcome their innate neophobia) and over a period of 30 consecutive days of daily vehicle consumption (n= 3-5 experimental group). Data are presented as mean ± SEM.

**VIDEO (QR Code or YouTube):**

**AWARD:** EPAA's 2021 REFINEMENT PRIZE

**STAGE OF DEVELOPMENT:** TRL 3
**IPR LEGAL STATUS:** Patent Pending n.° PCT/IB2021/053124 filed on 15/04/2021.
**OWNERSHIP:** The rights to the technology are held by the University of Coimbra and Polytechnic Institute of Coimbra.
**COLLABORATION SOUGHT:** Licensing for further developments or R&D partnership.

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