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Artificial gut/absorption simulator for evaluation of drug formulations dissolution

A device and method for simulating a digestive gut to evaluate drug delivery that incorporates simultaneous absorption with dissolution

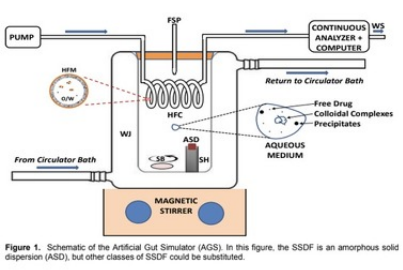
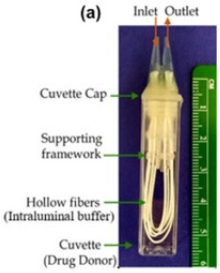


Figure 1. Schematic of the Artificial Gut Simulator (AGS). In this figure, the SSDF is an amorphous solid dispersion (ASD), but other classes of SSDF could be substituted.



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Category
All Technologies
Engineering & Physical Sciences/Instrumentation, Sensors & Controls
Life Sciences/Pharmaceuticals
Life Sciences/Research Tools

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IP Status: US Patent Issued; Patent No. 10,768,160

Applications

- Drug discovery and screening
- Dissolution testing

Key Benefits & Differentiators

- **Enables drug formulation screening:** This approach consumes less drug product due to a 333x smaller volume than traditional tests.
- **More representative measurement:** Incorporation of absorption more closely approximates dissolution in gut compared to standard tests in a closed system
- **Accurate measurement of bioavailable drug:** This approach differentiates between free drug and nano-sized drug aggregates or drug that is complexed to the excipient polymers, better representing actual bioavailable drug concentration in vivo.

Problem

Drug development is a billion-dollar activity and early selection of drug candidates and formulations with the required pharmaceutical properties could help reduce these costs. Solubility is a key property when developing a potential drug because it limits absorption and bioavailability. The standard USP dissolution test, which is intended and most frequently used for quality control, is neither optimal nor satisfactory for determining the efficacy of drug formulations in vivo, for two reasons. First, the system is closed with respect to the released drug, and any effects of drug absorption, which will tend to lower drug concentration and hence

reduce the rate of precipitation, are suppressed. Second, analytical techniques (e.g. HPLC) usually do not distinguish between free drug and nano-sized drug aggregates or drug that is complexed to the excipient polymers. While free drug is available for intestinal absorption, nano-aggregated or complexed drug probably is not. The analytical technique may significantly overestimate the ability of a formulation to provide drug in a supersaturated, highly bioavailable form. This combination of limitations results in the underestimation of drug efficacy and the overestimation of bioavailable drug. Therefore, there is a need for better systems and methods of dissolution testing of drug formulations that are accurate, efficient and inexpensive.

Solution

Prof. Siegel and his team at the University of Minnesota have developed an artificial gut simulator (AGS) (Image above) for more accurate and efficient dissolution testing. The AGS improves on standard USP dissolution tests by simulating drug absorption using a hollow fiber-based absorption module with large surface area and in-line monitoring. Together, these improvements provide a more representative assessment of drug formulations in vivo. The entire AGS is constructed in a 3 mL compartment, which reduces cost and waste associated with the standard dissolution test which takes place in a 1 L compartment. The simplicity of the AGS system and the need to use only a small volume and mass of the dissolution media and drug formulation, respectively, allows its applicability to screen solutions, suspensions and solid powder formulations such as amorphous solid dispersions in a high-throughput, cost-efficient, manner. The AGS has been demonstrated with a high aqueous solubility, BCS-I model compound caffeine and a poorly water-soluble, BCS-II model compound, ketoconazole. This technology is suitable for early screening of formulations during drug discovery research.

Phase of Development

TRL: 4-5
Prototype developed and tested with high and low solubility model compounds

Desired Partnerships

This technology is now available for:

- License
- Sponsored research
- Co-development

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Researchers

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References

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