# Appa: Agentic Preformulation Pathway Assistant



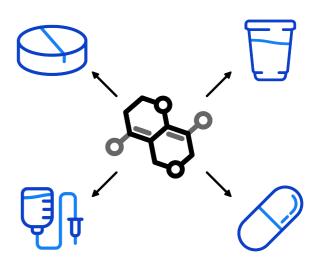
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The formulation of a small molecule in a drug development setting aims at enabling the delivery of a compound of choice within the desired dosage range and timing. This is usually achieved by combining several physico-chemical assays (e.g. solubility measurements) to probe which vehicles facilitates the diffusion of a molecule in a target environment.

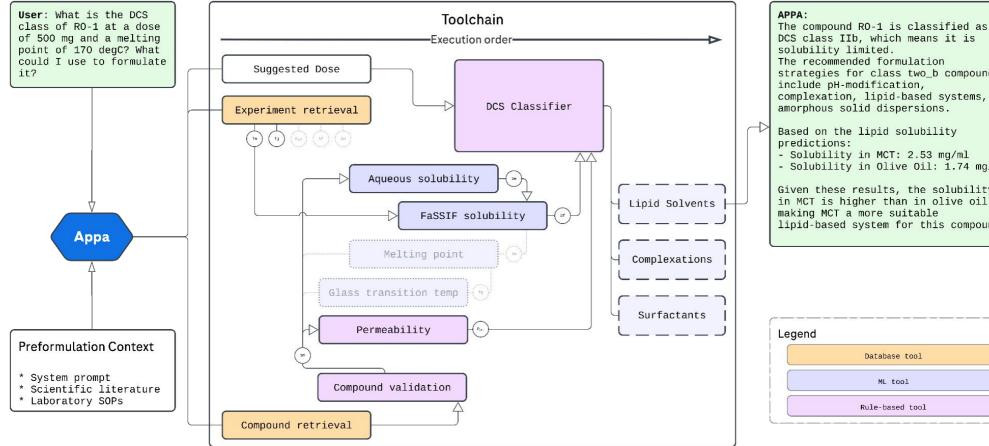
Appa presents a unified, intuitive interface through an LLM agent for the task of preclinical drug formulation<sup>1</sup>, enabling:

- Seamless access to experimental data and machine learning predictors
- Ability to respond to diverse scientific questions by chaining different tools
- A faster preformulation process through knowledge of experimental evidence, operating procedures and follow-up recommendations
- Clear decision making in the experiment planning



One substance - multiple formulations Crucial for efficacy and activity of a drug

## Example of a preformulation agentic pipeline



DCS class IIb, which means it is The recommended formulation strategies for class two\_b compounds include pH-modification, complexation, lipid-based systems, or amorphous solid dispersions.

Based on the lipid solubility

Solubility in MCT: 2.53 mg/ml - Solubility in Olive Oil: 1.74 mg/ml

Given these results, the solubility in MCT is higher than in olive oil, making MCT a more suitable lipid-based system for this compound.

ML tool Rule-based tool

#### **Evaluation**

- Task: Classification of a substance based on the Developability Classification System<sup>2</sup> (DCS)
- Scientific knowledge and understanding of multiple chemical properties required
- Testing of 500 virtual compounds based on structures from the ChEMBL<sup>3</sup> database

query:

What is the DCS class of SMILES [SMILES] at a dose of [DOSE] mg and a melting point of [MELTING POINT] degC?

Method	Accuracy	F1-micro
APPA	0.895	0.938
GPT-40 + Context	0.156	0.186

### **Future directions**

The workflow introduced in this work focuses on small - yet fundamental - task in a preformulation pipeline, which is the vehicle selection. In the following, we will highlight the next steps along two separate axes:

#### More ML models for formulation route selections

Our next steps will cover both the integration of further machine learning methods to cover broader vehicle spaces and rational next screening steps.

#### Multi-agentic interface to cover automatic screening planning

We plan on introducing a second agent, whose focus would be aimed at translating the experimental design into lab orchestration operations - to automate the preparation and the execution of solubility assays.

#### References

1: Vargason et al "Nature biomedical engineering 5.9 (2021): 951-967. 2: Butler and Dressmann, J. Pharm. Sci (2010) 99 12, 4940-4954

3: Zdrazil et al., Nucleic Acids Research (2024) **52** D1, D1180-D1192

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