SLU-PP-332 Dosing - myth vs reality, when science collides with the Bro's

After reading the mouse studies on SLU-PP-332 and the comments by the scientists who developed this compound AND having used this compound at the high end (500mcg) of the "bro dose", 3 times a day for several months I've concluded the Bro's are on the hype train and in this only for the money. The markup on this compound is astronomical.

There are a lot of reasons I do not agree with this microgram dose idea, and my reasons are supported by the current science on this interesting compound.

When people say they "did their research" my definition of research is different than many people. I've been involved in actual research, have worked with several PhD's over the years who had expertise in medical imaging, analog wave propagation (i.e., antennas) and chip design. Earning a PhD is a significant level of education. Those were people who had worked for Kodak, Samsung, and Blackberry before I met them and employed them.

Real research is very involved and requires years, if not decades of education and specialization in 1 field to be truly effective internet research, much less so especially when it comes to peer review.

Here are the chemical properties of SLU-PP-332 from a chemical supply company.

https://www.medchemexpress.com/slu-pp-332.html

As indicated in the monograph, and as the developers have indicated, it is NOT water soluble. I have tried every trick I have at my disposal and none of them worked to make it sustainably water soluble. You can make a suspension but that does not change the solubility issue. I expected that result but had to satisfy my own curiosity. It is important to be aware that when a compound is not water soluble, it has low bioavailability. Not even a sublingual dose will help, why? Because it's not water soluble.

Here are a few papers with the peer reviewed research on SLU-PP-332.

https://www.ahajournals.org/doi/10.1161/CIRCULATIONAHA.123.066542 https://www.sciencedirect.com/science/article/abs/pii/S0022356524171583 https://pmc.ncbi.nlm.nih.gov/articles/PMC11584170/#S7

There are no human studies/research on this compound, only mouse studies. I try not to rely on "bro-science" but occasionally it can be helpful. Online advice should be evaluated on the individual's motivation. There are some very smart influencers who sometimes exceed their level of education to collect an affiliate check.

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Note the dose in the mouse trials "SLU-PP-332 (50 mg/kg, i.p., twice per day for 28 days (or 12 days) induces fatty acid metabolism, reduces fat mass and improves glucose metabolism in diet-induced obesity mouse models"

There are some important bits of information in the above note from the clinical studies.

The dose used in mice can be converted to a human dose. In the studies, there are 2 other details to be noted, the composition of the dose, meaning how it was dissolved and how it was administered to improve bioavailability.

- 1) To convert the mouse dose to human, use the multiplier of $0.081 50 \text{mg} \times 0.081 = 4.05 \text{mg}$ per kg of body weight two times a day for humans.
 - a. At my weight of 64kg x 4.0mg = 259 mg (259,000mcg) TWICE a day.... when someone tells me an oral dose of 500 microgram (1/500th) is going to work, even 3 times a day (1,500mcg), I'm sceptical.
 - b. Which is why I'm currently taking 100mg orally (100,000mcg) and will up that to twice a day.
- 2) I.P. means Intraperitoneal injection into the body cavity of the mice.
 - a. the second highest way to improve bioavailability.
- 3) They also dissolved the SLU-PP-332 in DMSO before injection.
 - a. We have DMSO in our lab and that was one experiment to see if that would improve oral use. It does dissolve easily but when you put that mixture in water it is an issue. We tried several other techniques, including micronizing.

What to do about this? There is a dose issue, and a delivery issue, both driven by the bioavailability issue of this compound as it is currently formulated.

This compound was developed at Saint Louis University (SLU) and the developers have clearly stated is has very low bioavailability and they are working to improve that. This is the reason there are no human trials, and there won't be any on SLU-PP-332 as currently formulated.

Until there are actual human studies, the Bro's are pumping the heck out of this one for a ridiculous price. We offer 1gm for \$50 US, which would equal 2,000 (500mcg per dose) to 4,000 (250mcg dose) Bro doses which they sell for \$70 or more - $30mg = 120 \times 250mcg$ doses or $60 \times 500mcg$ doses.

If one were not interested in a 50mg dose, then purchase 1gm for \$50 and a 30mL dropper bottle, add 1 tiny scoop = 50mg of SLU-PP-332 to the bottle with 25mL of distilled water and be ahead of the game with 100x 500mcg doses in that bottle. One gram would provide $2,000 \times 500$ mcg Bro doses.

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Water solubility significantly affects the dose response and overall effectiveness of a compound or drug. Here are the key points regarding its impact:

- Poor water solubility often leads to low bioavailability because the drug cannot dissolve adequately in the aqueous environment of the gastrointestinal tract or bloodstream, which limits absorption into systemic circulation.
- Drugs that are poorly water soluble require higher doses to reach therapeutic plasma concentrations, potentially increasing side effects and cost.
- The rate of drug absorption is often limited by the dissolution rate, which is directly tied to solubility; low solubility slows dissolution, reducing absorption speed and total bioavailability.
- Poor solubility complicates formulation design and may cause variable efficacy due to inconsistent absorption.
- Enhancing solubility generally improves bioavailability, allowing lower doses and more consistent plasma levels, which improves dose response curves and pharmacological effects.
- Drugs with better solubility distribute more effectively in bodily fluids, improving therapeutic reach.
- For drugs with low solubility, advanced formulation techniques (e.g., nanoparticles, solubilizing excipients, self-emulsifying drug delivery systems) can improve dissolution and absorption, thereby enhancing dose response.

In summary, water solubility is a fundamental factor that can limit or enhance a drug's pharmacokinetic profile, impacting the required dose to achieve a therapeutic effect, the onset of action, and overall clinical efficacy.