# Development of a Simple Patient Centric Solid Dose Concept as alternative to Liquid Medicines

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## INTRODUCTION

Oral liquids and suspensions have several disadvantages relating to stability, accuracy of dosing and patient convenience[1]. Recently[2] there has been reported deaths from kidney injury in Indonesia of up to 100 children due to consumption of unregistered syrups that has led to the Indonesian authorities banning all syrups pending an investigation. Whilst the root cause of the problem was thought to be incorporation of liquids such as propylene glycol in the formulations, these sad events have placed into context the stark reality of the requirement to look for safer and more convenient alternatives to liquid based medicines.

We have investigated the utility of a novel ODT platform, UltraBurst® (UB) as a base that will enable formulators, consumers and pediatricians to offer simple alternatives to syrups and suspensions in a format that is safer, and more patient convenient. UB is a novel co-processed excipient platform consisting of mannitol, effervescent components and a super-disintegrant.

## AIMS and OBJECTIVES

UB as a base was investigated for a range of API's formulated as tablets that could subsequently be dropped into various liquids- water, apple juice, mango juice, yoghurt and syrup (added to a 5ml spoon) giving a convenient and palatable alternative to liquid medicines. The performance of the UB platform was also compared to other marketed ODT platforms. API's considered included low dose eg loperamide HCl 2mg, taste masked Diphenhydramine (1.25mg) as well as higher dose API's such as taste masked paracetamol (doses of at least 60mg). Several Tablet weights were investigated, mini tablets (10-20mg), smaller (50mg) and standard sized tablets (400mg).

## MATERIALS and METHODS

Flash ODT (FODT) formulations were formulated as placebos and with 3 different model API's –Loperamide HCl (LOP), Diphenhydramine (DPH) and Paracetamol (APAP). The performance of the UB platform was also compared to other ODT platforms, indicated as platforms P1-P4.All formulations were manufactured via a Direct Compression process requiring simple sieving of components, followed by blending and lubrication step, then compression on a Pacific Rotary Tablet Press. The formulations were compressed using the requisite tooling at the appropriate compression force and the resultant tablets were then assessed for the physical properties indicated in Table 2. Resultant tablets were then added to a range of different palatable liquids on a 5ml spoon and the dispersion event observed, the time and extent of spread versus times were recorded as video.

## RESULTS AND DISCUSSION

**Table 1** shows a typical concept formulation of UB tablets 50mg in weight containing 20mg of APAP (in the form of taste mask Actimask®). **Table 2** shows the physical properties of the tablets. The tooling used was 6.2mm round FFBE.

Table 1

| | |
|---|---|
| Weight (mg) | 50.1 |
| Thickness (mm) | 1.45 |
| Hardness (N) | 16 |
| Friability (%) | 0.22 |
| DT (sec) | 4 |
| Comp Force (kN) | 3.4 to 3.8 |

Table 2

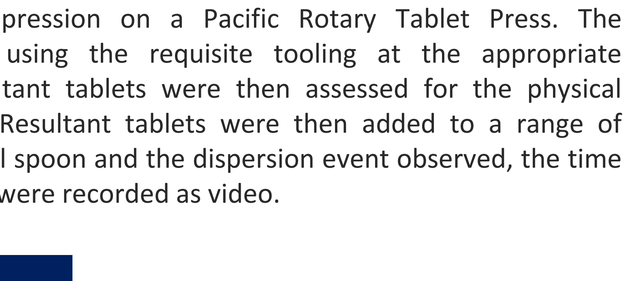
| material | mg/tab |
|---|---|
| Actimask APAP | 22.0 |
| Ultraburst | 25.9 |
| Raspeberry Flavour | 0.65 |
| sucralose | 0.65 |
| magnesium stearate | 0.75 |
| total | 50.0 |

As shown in Figure 1, UB based placebo tablets show significantly faster and more complete dispersion versus the other systems studied and so is the most viable base for this approach.

Dispersion of UB based placebo tablets is also faster in the lower viscosity apple juice but still gives an acceptable result in the mango juice.

### COMPARISON OF ODT PLATFORM

**Figure 1 –** shows the dispersion of the different ODT base 100mg placebo tablets in apple juice after 25 secs.



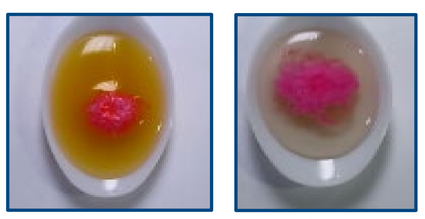
UB (pink left) vs P1 | UB vs P4

UB vs P3 | UB vs P2

### PERFORMANCE OF ULTRABURST®:

**I. Impact of viscosity of liquid media on the dispersion**

**Figure 2** – shows the effect of the viscosity of the liquid media on the dispersion. Images are of 100mg UB placebo tablets dispersed in mango juice and apple juice after 32 and 27 secs respectively.



Mango Juice | Apple Juice

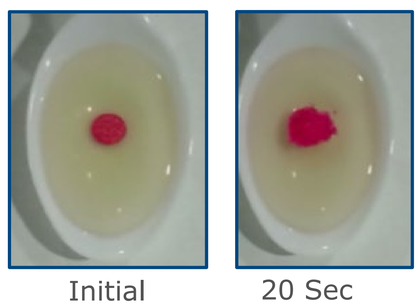
**II. Impact of Tablet weight on the dispersion**

**Figure 3(a)** – shows the effect on tablet size (weight) on dispersion. Images are of UB placebo tablets (400mg and 100mg) dispersed in water after the indicated dispersion time.

400mg at 25 sec | 100mg at 20 sec

Complete dispersion was seen at the higher 400mg tablet weight after only 25 sec.

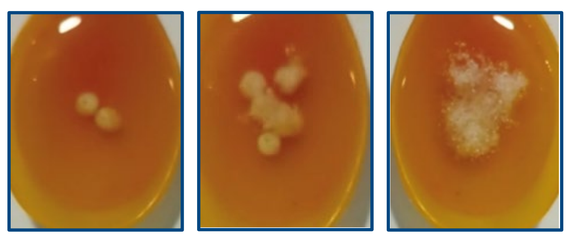
**Figure 3(b)** – shows the UB based APAP 50mg tablet detailed in Tables 1 and 2 at initial time point and after 20 secs when dispersed in apple juice.



Initial | 20 Sec

Inclusion of the active has not significantly slowed the dispersion.

**Figure 3(c) –** shows images of a UB based taste masked DPH mini tablets containing 1.25mg of taste masked DPH added to apple juice at 4, 10 and 18 sec respectively.



Mini tablets disperse rapidly and completely within 20 secs. Up to 10 mini tablets could easily be incorporated in one spoon.

## CONCLUSION

We have demonstrated a novel and simple means of converting current liquid medicines into FODTs that when added to palatable liquids in a 5ml spoon such as apple juice, mango juice, syrup or even water, will quickly and completely disperse within less than 30 seconds to give a slurry of dispersed API that could easily be given to a child. The concept is feasible across a wide range of tablet sizes (10 – 400mg weights investigated) thus enabling both low and high dose API's to be dosed via a number of tablets added at each required dosing time. The viscosity of the liquid will slow the time for full dispersion, however even in the higher viscosity mango juice studied complete dispersion in around 30 seconds was possible. The dispersion propensity is significantly slower and incomplete with the other systems studied. This concept could considerably improve paediatric treatment by eliminating the need for liquid medicines and the disadvantages associated with the liquids. Choice of juice needs to be considered by consulting a healthcare professional, as some juices (Eg: Grape juice) are known to interfere with the metabolism of certain drugs[3].

## REFERENCES

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