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CASE STUDY | ORAL DOSAGE

**Two-component simple platform for orally disintegrating tablet (ODT) application**

## SITUATION

Orally disintegrating tablets (ODT) are solid dosage forms which disintegrate/melt rapidly when placed on the tongue and do not require water for swallowing. ODT formulation was introduced to the market with the goal of better patient compliance, further gaining popularity as an alternative Rx and over-the-counter (OTC) oral dosage forms, as well as nutraceuticals. ODTs are particularly suitable for consumers with dysphagia (difficulty in swallowing), specifically pediatric and geriatric populations, or for cases when compliance is a known issue, such as mentally disabled patients. ODTs are also intended for convenience as an "on-the-go" medication when water is not available or when consumption of water/liquid is not desired, for example persistent nausea. ODTs are preferred over chewable tablets in certain situations such as when chewing is difficult or painful. Improved bioavailability of active ingredients in orodispersible formulations is possible due to pre-gastric absorption, reducing first-pass liver and gastric metabolism, which is beneficial when faster onset of action is required, e.g. emergency or pain medications, or for drugs that degrade or metabolize intensively when digested.

As per American (USP) and European (EP) pharmacopoeias, ODTs should weigh 500 mg or less, disintegrate in less than 30 (USP) or 180 seconds (EP) in 2 mL of available saliva, and have friability of ≤ 1%. In order to satisfy prompt disintegration requirement, the tablet is designed to have a highly porous matrix for quick entrance of saliva, which is usually achieved by incorporating a combination of disintegrants or superdisintegrants. Various technologies are used in ODT manufacturing: freeze-drying, direct compression (at low forces), cotton candy, etc. Amongst them, direct compression is the most cost-effective and easy-to-handle on standard equipment practice, resulting in low-friability tablets. Mannitol is the chosen filler in commercially available ODT platforms. It has mild sweet pleasant taste with a cooling effect in the mouth, and is water soluble but not hygroscopic. Other excipients, in particular disintegrants and lubricants, may negatively affect mouth feel and in addition are known to contain reactive groups and impurities that can reduce ODT shelf-life.

## CHALLENGE

Simple inert direct compression platform for Orally Disintegrating Tablet (ODT) formulations is in demand for development and re-formulation of pharmaceutical and nutraceutical products.

## SOLUTION

PEARLITOL® Flash is a platform composed of only two long-established ingredients of natural origin – mannitol and maize starch, enabling production of high quality ODT by direct compression.

**PEARLITOL® Flash key benefits:**

- PEARLITOL® Flash, mannitol and starch compound, has superior wettability compared with other platforms, resulting in fast self-disintegration (no need for superdisintegrants).
- Low lubricant level (0.4% magnesium stearate) is sufficient for direct compression process.
- PEARLITOL® Flash based ODTs melt in the mouth in seconds with a very creamy, smooth texture resulting in a uniquely pleasing taste experience.
- PEARLITOL® Flash complies with major market pharmaceutical and food regulations and can be used for pharmaceutical and neutraceutical applications.

## RESULTS

**1. ODT excipient platform impacts disintegration time and mouthfeel:**

300 mg ODT placebos were made using ready-to-use ODT platforms at two hardness values (50N and 90N) and their disintegration time evaluated (Table 1).

- Tablets hardness had no effect on the in vivo disintegration time for PEARLITOL® Flash, mannitol and starch compound (P1), while for the other platforms (P2, P3, and P4) there was noticeable variation as a function of hardness. P1 superior wettability in comparison with other platforms is accountable for this outcome.
- 24-trained panelists were asked to express their opinion on mouthfeel and disintegration of placebo ODTs (Table 1). Volunteers reported that PEARLITOL® Flash (P1) placebo ODTs had a sweet, creamy, smooth texture that disintegrates fast. Synthetic origin of some tested platforms affected organoleptic volunteer experience.

| | Platforms composition | In Vivo Disintegration time [At tablet hardness 50N/90N] | Mouthfeel |
|---|---|---|---|
| P1 | **PEARLITOL® Flash:**<br>Mannitol<br>Maize Starch | 36/40 (sec) | Sweet taste creamy, smooth and fine texture |
| P2 | Mannitol<br>Crospovidone<br>Polyvinyl acetate<br>Povidone (PVP)<br>Sodium Lauryl Sulfate (SLS) | 58/82 (sec) | Creamy and sticky texture |
| P3 | Mannitol<br>Crospovidone<br>Microcrystalline cellulose<br>Colloidal silicon dioxide<br>Fructose | 119/242 (sec) | Not very sweet, takes too long to melt |
| P4 | Mannitol<br>Croscarmellose | 199/186 (sec) | Takes too long to melt, hard center |

Table 1 - Disintegration time and mouthfeel of placebo ODTs.

**2. ODT excipient composition plays a significant role in physicochemical stability of formulation:**

Stability of model drug benzocaine, prone to oxidation and degradation, has been evaluated in ODTs formulated with various platforms under standard and accelerated conditions. ODTs were formulated with 6% benzocaine, 1.5% magnesium stearate (lubricant), and 92.5% of respective ODT platform (Table 2).

- ODT formulated with PEARLITOL® Flash, mannitol and starch compound, (P1) had excellent shelf-life under standard and accelerated condition over 6 months of storage.
- Physical stability was impacted by reducing sugar (fructose), superdisintegrants, and MCC.
- Chemical stability was impaired by reducing sugar (fructose) and reactive agents (peroxides, formic acid, and formaldehyde) in crospovidone, PVP or PVA.

| | Platforms composition | Benzocaine Stability in ODT (model Active) | ODT appearance Day 0 [100N/20kN] | ODT appearance Day 180 40°C/75 %RH [100N/20kN] |
|---|---|---|---|---|
| P1 | **PEARLITOL® Flash:**<br>Mannitol<br>Maize Starch | Within range/stable [0 – 180 days] |  |  |
| P2 | Mannitol<br>Crospovidone<br>Polyvinyl acetate<br>Povidone (PVP)<br>Sodium Lauryl Sulfate (SLS) | Within range/stable [0 – 180 days] |  |  |
| P3 | Mannitol<br>Crospovidone<br>Microcrystalline cellulose<br>Colloidal silicon dioxide<br>Fructose | Degradation at day 30 @ 40°C/75 %RH |  |  |
| P5 | Mannitol<br>Xylitol<br>Microcrystalline cellulose<br>Crospovidone<br>Magnesium aluminosilicate<br>Dibasic calcium phosphate anhydrous | Within range/stable [0 – 180 days] |  |  |

Table 2 - Physicochemical properties of ODT containing model drug benzocaine.

## CONCLUSION

PEARLITOL® Flash, mannitol and starch compound, offers inert stability, fast disintegration and superior organoleptic properties, allowing complex ODT formulations to become simple. PEARLITOL® Flash shows beneficial stability and patient compliance characteristics when compared to other inert natural formulations.

## REFERENCES

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