

Optimum taste of liquid paracetamol can help in compliance and acceptability among pediatric patients with pain and fever

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Background

- Paracetamol (acetaminophen) is an analgesic and antipyretic used to treat mild to moderate pain and reduce fever in patients aged ≥ 1 month.¹
- Liquid formulations (solutions/suspensions) are favored for administration in young children (< 5 years),² but this group is particularly averse to the bitter tastes associated with liquid medicines, including paracetamol,² hence bitter taste is masked by sucrose and/or artificial sweeteners, and flavorings.³
- Rejection of medication (spitting or vomiting) can lead to dosing errors such as underdosing (leading to reduced effectiveness) or overdosing on attempted re-administration (leading to toxicity).
- Hence, poor palatability may contribute to symptom persistence, worsening of condition, or need for additional medication/doctor visits/hospitalization.³
- We reviewed literature on the impact of taste of liquid paracetamol formulations on compliance and acceptance in pediatric patients.

Methods

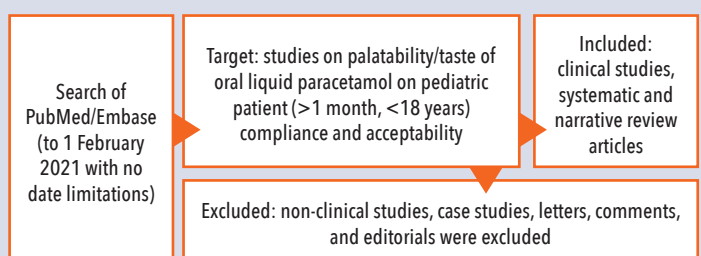


FIGURE 1. Search methodology.

Results

Taste perception is driven by patient factors

- Taste is experienced as a response from taste receptor cells together with the processing of olfactory and visual stimuli, and memory.⁴
- Patient factors that modulate taste perception include:
 - Age: Care is needed in interpreting taste-preferences of children < 5 years, who might not be able to clearly express their preferences
 - Cultural background
 - Phenotype and genotype; influences sensitivity to bitterness/sweetness

Mechanism of taste perception enables masking of bitterness by sweetness to improve palatability

- Sweet (T1R2) and bitter (T2R2) taste transduction mechanisms share common signaling pathways (Figure 1).⁵
- Bitter taste is modulated by addition of sugar or sweeteners and used to mask bitterness of liquid medications to improve their acceptability.²
- Sweet solutions may have indirect pain relieving effects in infants (< 1 year); however, there is limited evidence for analgesic effects of sweet taste in school-aged children.⁶

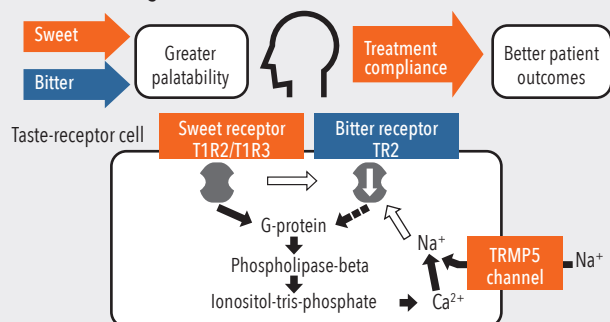


FIGURE 1. Sweet and bitter taste transduction mechanisms share common signaling pathways. Bitter/sweet receptor activation is associated with hydrolysis of G-proteins, which activate phospholipase- β and ionositol-tris-phosphate to increase intracellular free Ca^{2+} . This causes Na^{+} to inflow via opening of TRPM5 channels. Inhibition of bitter perception by sweeteners might occur at the receptor level or downstream to receptor activation. Adapted from reference 5.

Sweet tasting medications are preferred among children

- A 2013 systematic review of the literature on palatability and swallowability of oral dosage formats in children (< 18 years),⁷ highlighted a 2013 observational study of drug administration practices among 206 children (6–12 years) evaluated by their caregivers:⁸
 - Poor palatability influenced drug acceptability
 - Vomiting of medicines (unspecified) was noted to be a problem by almost all healthcare workers (192/202, 95%)
 - Caregivers (155/194, 80%) and children (186/204, 91%) preferred sweet to bitter-tasting medication

Both taste and flavor may influence acceptability and compliance

- A 2019 observational study examined acceptability of different liquid formulations of paracetamol in pediatric patients.⁹
 - A 2.4% strawberry-flavored oral suspension had more positive acceptance than a 300-mg powder for oral suspension (Figure 2).
 - Children administered a flavored oral suspension were younger than those administered powder for oral suspension.
 - Nevertheless, children > 5 years tended to receive powder for oral solution despite a lower rate of dose fully taken and a higher rejection rate than the oral suspension.

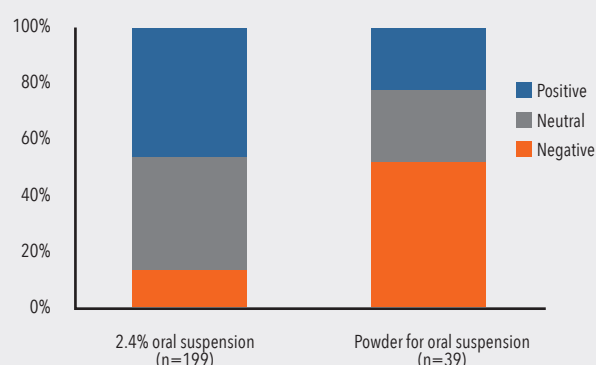


FIGURE 2. ClinSearch Acceptability Score Test of two paracetamol liquid formulations.

- A 2019 observational study of 145 children (mean age of 5.7 ± 2.9 years) also found that higher taste and smell scores (based on questionnaires with 5-point facial hedonic scale) were associated with a decrease in spitting behavior.¹⁰

Conclusions

Liquid paracetamol has a bitter taste and formulations may be rejected by children, leading to poor treatment outcomes. This review finds that masking of bitter taste with sweeteners and/or flavorings can improve acceptance. However, individual taste perception also influences acceptability and opportunities remain to further optimize liquid paracetamol formulations and enhance their acceptability. Age, regional and ethnic variations should be considered when developing new liquid paracetamol formulations for children.

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