Sensory Analysis of 160 Investigational Drugs:

A Framework for Assessing Taste-Masking Difficulty

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Abstract

Ensuring palatability is critical to patient acceptance, particularly for pediatric and dysphagic populations. However, the taste-masking challenge of active pharmaceutical ingredients (APIs) is rarely characterized early in development to inform patient-centric formulation design.

This study presents a retrospective analysis of 160 APIs in Senopsys' FlavorMetrics[SM] database, evaluated using the Flavor Profile Method, an ISO/ASTM sensory method that uses trained assessors to quantify taste, aroma, mouthfeel, and texture.

Bitter taste was the primary attribute in **65%** of APIs, followed by malodors (**9%**), trigeminal irritation (**5%**), and sour/salty tastes (**4%**), while **15%** of APIs were flavorless. Notably, over **90%** of APIs exhibited multiple aversive attributes.

Time-intensity analysis enabled APIs to be classified according to taste masking difficulty and provided a framework for matching formulation strategy to the specific sensory challenges of each API.

These findings demonstrate that early, quantitative characterization of aversive sensory attributes is essential to guide dosage form selection and optimize taste masking strategy.

Introduction

Flavor integrates taste, aroma, mouthfeel, and texture, and many APIs possess aversive sensory attributes that can reduce acceptance and adherence, especially in pediatric populations.

Tablets and capsules are unsuitable for pediatrics and populations that have difficulty swallowing, however alternative forms often prolong oral residence time and exacerbate aversive flavors. Accordingly, FDA and EMA require development of palatable, age-appropriate formulations and the AAPS Pediatric Formulations Task Force recommends first identifying and quantifying aversive flavor attributes to guide taste-masking strategy.

Sensory analysis using human subjects remains the accepted approach to evaluate flavor, as current in vitro models lack reliable correlation with human perception.

This study retrospectively analyzed the flavor profiles of 160 investigational drugs indicated for both common and rare diseases (Figure 1) and a variety of dosage forms (Figure 2).

Figure 1. Therapeutic Areas

Cardiology	Immunology	Nephrology
Endocrinology	Infectious Diseases	Neurology
Gastroenterology	Oncology	Rare Diseases
Genetic Disorders	Pulmonary	Sleep
Hematology	Psychiatric Health	

Methodology

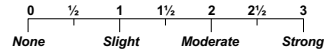
Figure 2. Intended Dosage Forms

3D Printed Tablets	Nasal Sprays	Oral tablets
Chewable Tablets	Nebulized Liquids	Soft chews
Dry Syrups	Minitablets	Solutions
Films	Multiparticulates	Sprays
Gummies	Oro-adhesive tablets	Suspensions

Samples were analyzed by Senopsys using the Flavor Profile Method (Figure 3), an ISO/ASTM sensory methodology. Trained and experienced adult assessors identified and quantified the perceived intensity of flavor attributes in the initial flavor and at 1, 3, 5, 10, 15, 20, 25, and 30 minutes in the aftertaste.

Figure 3. Flavor Profile Method Summary

1. **Flavor Attributes:** Identify the perceived flavor attributes: taste, aroma, mouthfeel and texture
2. **Intensity:** Measure the intensity of each attribute using a scale established with chemical reference standards:



3. **Aftertaste:** Measure all sensations remaining in the aftertaste at selected intervals.

All flavor modalities were assessed – taste, aroma, mouthfeel, and texture. Attribute intensity was measured using a 7-point intensity scale ranging from 0 to 3. A score of 1 represents the recognition threshold, the minimum intensity detectable by patients. Consequently, successful taste masking was defined as reducing aversive sensory attributes below the recognition (palatability) threshold. All evaluations were conducted in accordance with ICH Good Clinical Practice guidelines.

Results

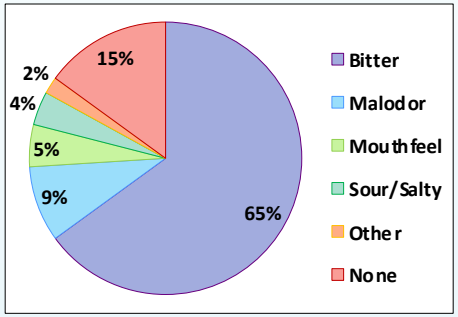
The primary aversive sensory attributes of the 160 APIs are shown in Figure 5. Bitterness was the most common aversive attribute measured in 65% of the APIs. Aversive aromas were the next most common, found in 9% of APIs. Some descriptors of these malodors are shown in Figure 4.

Figure 4. Aversive Odor Descriptors

Acetate	Fecal	Peroxide
Acetone	Fermented	Petroleum
Amine	Fishy Amine	Phenolic
Burnt Polyethylene	Geosmin (Moldy)	Resinous
Butyric Acid	Heptane	Smokey
Candle Wax	Iso-Propyl Alcohol	Sulfide
Ethanol	Musty	Thiol
Ether-Like	Oxidized Oil	Wet Cardboard

Results *(cont.)*

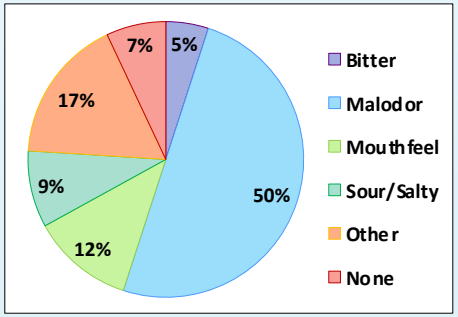
Figure 5. Primary Aversive Attributes of 160 APIs



Approximately 5% of the APIs produced mouthfeels such as trigeminal irritation (e.g., burning, numbing). A smaller subset were sour or salty (4%). None were found to be sweet. Fifteen percent of APIs were "bland" tasting with no measured aversive attributes.

Most APIs exhibited more than one aversive sensory attribute, with secondary challenges summarized in Figure 6. Identifying all attributes is key to a successful formulation strategy.

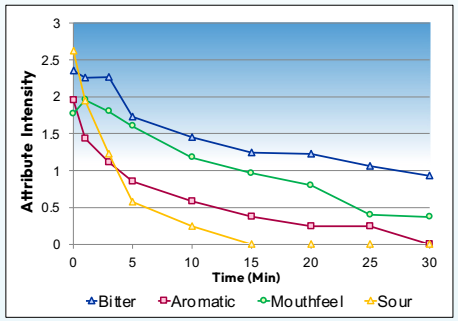
Figure 6. Secondary Aversive Attributes of 160 APIs



Because the persistence of aversive attributes in the aftertaste contributes significantly to overall palatability, time-intensity analysis was used to characterize flavor duration. Plotted in Figure 7 are the mean time-intensity profiles for bitter, aromatic, mouthfeel, and sour attributes across the entire API dataset. The region of the chart shaded in blue represents intensities above the recognition threshold (intensity = 1) and is most critical to palatability. Among the common aversive attributes, **bitterness had the longest mean aftertaste**, whereas aromatic and sour attributes generally declined more rapidly.

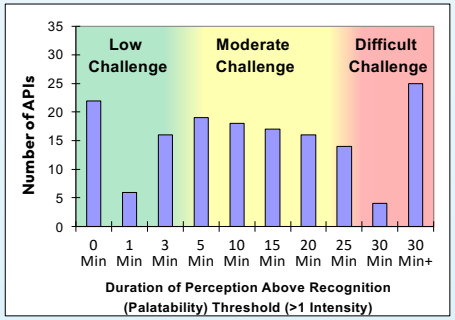
Discussion

Figure 7. Mean Time-Intensity by Aversive Attribute



Aftertaste duration was used to categorize taste-masking difficulty of the APIs based on excipient functionality (Figure 8). APIs with aversive attributes persisting for 0–3 minutes (n = 46) were classified as a low taste-masking challenge. APIs that persisted for 5–25 minutes (n = 84) represented a moderate challenge, while those that remained perceptible for 30 minutes or longer (n = 30) were highly difficult to taste mask.

Figure 8. Taste Masking Difficulty of 160 APIs



Conclusions

Human taste assessment should begin **immediately after successful Phase 1 studies**, when clinical viability is established and formulation decisions become critical.

Quantitative assessment of flavor modality, intensity, and duration enables stratification of APIs by taste-masking difficulty and provides a framework for dosage form selection and implementation of targeted taste-masking strategies, including flavor systems, encapsulation, complexation, and particle coating.