

TASTE MASKING IN ORAL DOSAGE FORMS: EXPLORING CONVENTIONAL AND NANOTECHNOLOGY-BASED APPROACHES

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ABSTRACT

Patient compliance is essential for successful pharmacotherapy, and oral medications that taste bad, especially to young and elderly patients, are often the reason for non-compliance. Taste masking is therefore crucial for improving patient adherence and therapeutic outcomes. This review looks at a variety of taste-masking techniques, including both well-known and innovative technologies based on nanotechnology. Nanotechnology offers promising alternatives to traditional methods such as coating, granulation, microencapsulation, and the addition of sweeteners, which have disadvantages such as uneven masking and potential effects on medication efficacy. These methods include the use of nanocarriers, liposomes, nanoparticles, and nano emulsions. These innovative techniques can successfully mask undesirable flavors, enhance the delivery of oral medications, and ultimately improve patient compliance and quality of life.



INTRODUCTION

Patient compliance is crucial for successful health outcomes, especially for chronic diseases.^{(1) (2)} Key attributes include self-care behaviors, adherence to health recommendations, and collaboration with healthcare professionals^(1, 2). Factors influencing compliance include motivation, education, trust, treatment complexity, and communication quality.^(3, 4) Modern perspectives emphasize patient empowerment and shared decision-making.^(5, 6) Technological interventions like telehealth can enhance compliance, but effectiveness depends on individual factors and ongoing support.^(2, 7)

Impact of Poor Compliance on Treatment Outcomes

Noncompliance with medical treatment has a significant impact on health outcomes, including a range of illnesses.⁽⁸⁾ In chronic conditions like thalassemia, noncompliance with iron chelation medication increases the risk of complications, liver and heart damage, and a reduced quality of life.⁽⁹⁾ When active surveillance measures are not followed, the risk of prostate cancer metastases and treatment failure increases.⁽¹⁰⁾ Drug-resistant strains of tuberculosis, increased transmission,

and prolonged illness are the outcomes of noncompliance.^(7, 11) Increasing adherence through patient education and support is essential for improved health outcomes and reduced healthcare costs.^(1, 12, 13)

Consequences in Chronic Disease Management

Managing chronic diseases improves clinical outcomes, increases medication adherence, and reduces hospital readmissions for conditions like diabetes, heart failure, and respiratory disorders.⁽¹⁴⁾ Community pharmacist-led care and self-management programs improve quality of life, self-efficacy, and depression symptoms.⁽¹⁶⁾ Policies that provide incentives to people and healthcare professionals can raise awareness of diseases.⁽¹⁴⁾ Although team-based treatment models and eHealth solutions facilitate self-management, problems with long-term interventions, inconsistent results, and financial gains outside of diabetes care persist.^(14, 15, 18, 19)

Effect on Medication Efficacy and Symptom Control

The efficacy of drugs and symptom management are linked to adherence, self-efficacy, and patient empowerment.^(19, 20) High self-efficacy promotes increased medication adherence in conditions like depression, diabetes, and hypertension,^(21, 22/23) which enhances clinical outcomes and symptom management.^(24/25) Interventions such as self-management programs, adherence treatment, and digital health tools can improve blood pressure, glycemic control, and depressive symptoms.^(20, 23, 24, 26)

Noncompliance with treatment increases health risks and costs associated with psychiatric disorders.^(27, 28) Poor adherence leads to higher rates of relapse, more hospital stays, and a lower quality of life, especially in conditions like severe depression and schizophrenia.⁽²⁹⁾ Furthermore, it exacerbates comorbidities, increasing the strain on healthcare systems, lengthening hospital stays, and driving up medical costs.⁽³⁰⁾ Socioeconomic factors make these risks even worse.⁽³¹⁾ Patient-centered therapies and integrated care approaches are crucial for enhancing adherence and quality of life.^(28, 29, 32)

Patient compliance in healthcare is influenced by a number of factors, including communication from healthcare professionals, motivation, and understanding of their condition.⁽³³⁾ Strong relationships, effective communication, and patient satisfaction are all linked to better adherence.⁽³³⁾ Social, psychological, demographic, and socioeconomic factors also affect adherence.⁽³⁵⁾ Social support systems, past medical experiences, health opinions, the complexity of the treatment plan, and patient satisfaction are all significant indicators.⁽³⁶⁾ These factors are the focus of the most effective patient adherence-promoting interventions.⁽³⁵⁻³⁷⁾

Treatment compliance is significantly impacted by the unpleasant taste of oral medications, especially for children and older adults⁽³⁸⁾. Strategies include things like bitter blockers, flavorings, and sweeteners.⁽³⁹⁾ Innovative techniques like lipid microspheres and nanospheres reduce bitterness and increase palatability.⁽⁴⁰⁾ Mini-tablets and orodispersible dosage forms are recommended for these people.⁽⁴²⁾ Optimizing carrier materials, drug-to-carrier ratios, and flavoring agents is essential⁽³⁸⁾. The combination of functional, physical, and biochemical techniques drives improvements in oral medication efficacy and acceptance.^(39, 40, 43)

Types and Mechanism of Taste

Umami, sour, bitter, salty, and sweet are the five flavors that humans can detect.⁽⁴⁴⁾ These sensations are detected by specialized receptor cells in taste buds, which are primarily found on the tongue.^(45, 46) The receptors trigger a sequence of intracellular signaling events that trigger the release of neurotransmitters and activate sensory nerves^(47, 48). In recent years, new pathways for neurotransmitter release and sour taste have been identified.⁽⁴⁹⁾ Taste receptors also play a role in metabolic regulation and immunological defense.^(50, 51) Understanding taste mechanisms can aid in determining potential treatment targets as well as dietary and health-related factors.^(45, 47, 48)

The Physiology of Taste Perception and the Need for Taste Masking

Taste-active chemicals interact with taste bud receptors and send nerve impulses to the brain,

causing taste perception, a crucial physiological function.⁽⁵²⁾ It significantly affects food choice, nutrient intake, and health.^(40, 53) However, unpleasant tastes in drugs and traditional therapies can reduce patient compliance and

effectiveness.^(44, 54) To address this, a variety of taste-masking strategies have been developed, including computer modelling, bitter blockers, sweeteners, physical barriers, nanocarrier systems, and human taste panels.^(40, 55, 56)

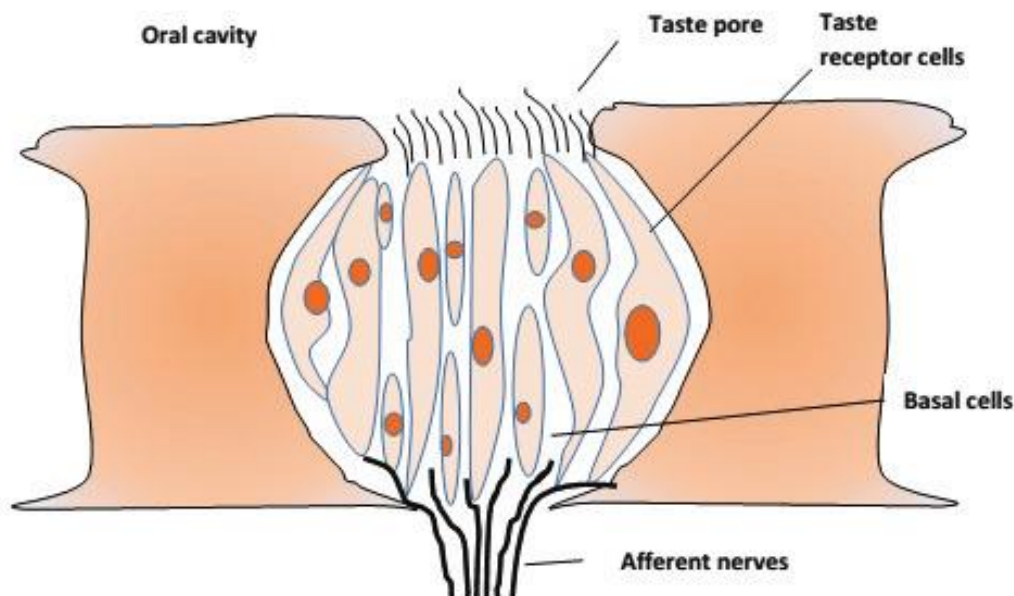


Fig. 1. Taste buds regulate the four main senses of salt, sweetness, sourness, and bitterness. Damage to the taste buds may lead to poor nutrition and hunger. Taste masking is one method to lessen the detection of unpleasant tastes, such as bitter ones. Pharmaceutical formulations with modified taste characteristics often yield higher profits. To effectively conceal a taste, one must understand how excipients interact and change across the tongue. Taste masking can be caused by either central or peripheral cognitive connections.

The mechanism of taste perception varies for different tastings: Salty and Sour

The perception of sour and salty flavors is influenced by specialized ion channels in taste receptor cells.⁽⁴⁴⁾ Epithelial sodium channels (ENaC) detect salty flavors, whereas direct proton entry (OTOP1 channel) detects sour ones.⁽⁵⁷⁾

Interactions between salty and sour stimuli can alter taste perception; ⁽⁵³⁾ higher sour concentrations reduce salty taste, while lower sour concentrations increase it^(47, 58). Advances in electrophysiology and molecular modelling have increased understanding.^(47, 59, 60)

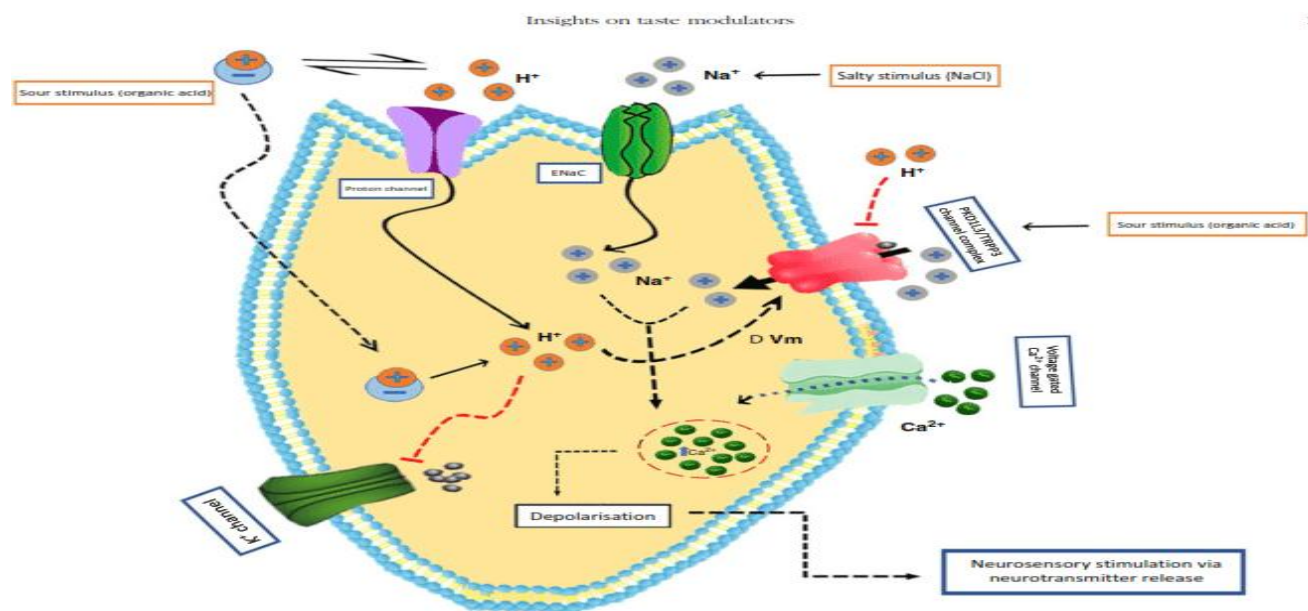


Fig. 2. PKD2L1 and PKD1L3 are two of the many channels that taste bud cells use to identify sour and salty flavours. Salt flavour is produced by the epithelial-type sodium channel (ENaC), while sour flavour is caused by protonated acids. The primary salt stimulation causes depolarization.

Sweet, Bitter, and Umami

G protein-coupled receptors (GPCRs) on taste buds are responsible for detecting umami, bitter, and sweet flavors. Sweet and umami flavors are detected by type 1 taste receptors (TAS1R), while bitter flavors are detected by type 2 receptors.⁽⁶¹⁾ When these receptors trigger intracellular

signaling events, taste information is sent to the brain and neurotransmitters are released. Structural studies have demonstrated that different receptors have unique activation pathways⁽⁶²⁾, and both physiological and genetic factors can influence sensitivity and preference for different tastes.^(44, 61, 63, 64)

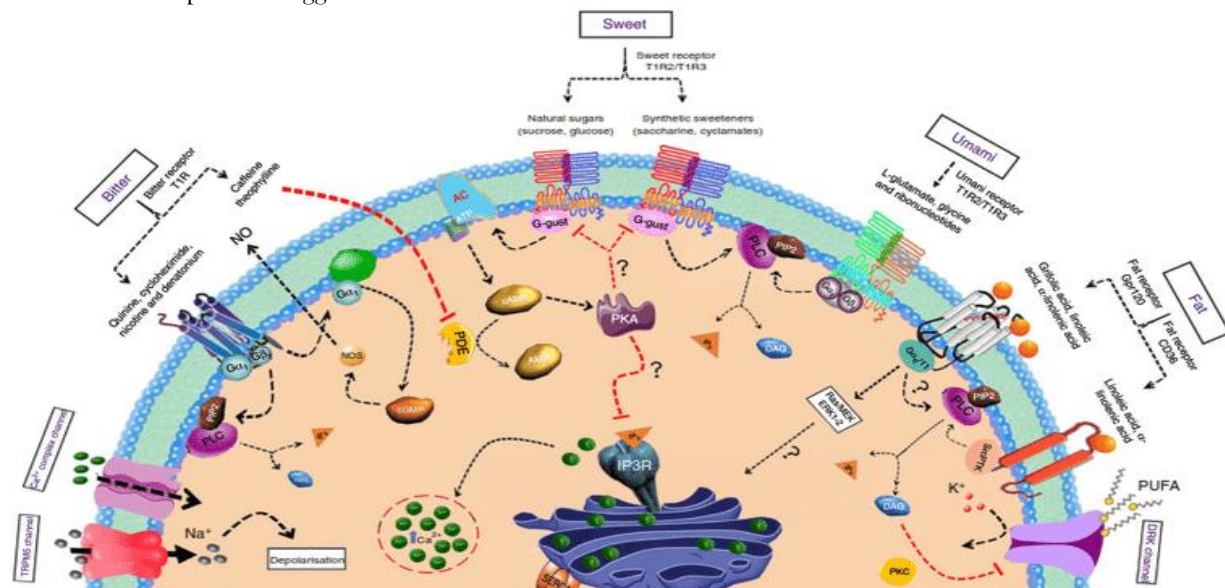


Fig. 3. To distinguish between sweet, umami, bitter, and fat flavours, taste buds use GPCR and CD36. Activated signals are sent to PLC and AC, which generate AMP and diacylglycerol, respectively.

Table 1 Pharmaceutical Importance of Taste Masking

Strategy / Aspect	Description	References
The Value of Masking Flavors	vital for oral medications because unpleasant or bitter flavors can significantly reduce patient adherence, particularly in younger and older patients.	(39) (40, 56)
Strategies Used	comprises a range of techniques, including Barriers based on lipids Methods of coating Complexes of inclusion Flavors of Sweeteners Advanced systems for nanocarriers	(65)
Factors to Take into Account When Choosing a Strategy	The following factors influence the flavor-masking strategy choice: Particular characteristics of the pharmaceutical active ingredients (APIs) The drug's desired release profile	(66)
Developments in the Assessment of Taste	The analysis and improvement of flavor-masking techniques are always being enhanced by technological developments.	(55, 67, 68)

Taste Masking Strategies

Taste masking strategies are crucial in pharmaceutical formulation to improve patient compliance, especially for drugs with unpleasant tastes.⁽⁴⁰⁾ Common methods include adding sweeteners, flavors, and bitter blockers, but they might not be sufficient for complex formulations or very bitter drugs.^(55, 69) Advanced techniques include ion-exchange resins, nanocarrier systems, inclusion complexes, physical barriers, chemical changes, and regulating drug release patterns.^(39, 70) The patient group, the intended release profile, and the drug's properties all affect the procedure choice.^(55, 56, 71)

Evaluation and Development

The significant disparities in taste perception among children, healthy adults, and the elderly have an impact on nutrition and medication compliance.^(72, 73) Children's less developed ability to discriminate between bitter tastes, particularly those between the ages of 4 and 8, makes drug formulation more challenging.⁽⁷⁴⁾ Older people's taste perceptions are less intense and integrated because of changes in multimodal brain processing.⁽⁷⁵⁾ Oral sensation and taste receptor activation are further diminished as people age

due to biological factors like decreased salivary flow and mucin composition,^(72, 75) which may affect nutrition and quality of life.⁽⁷⁶⁾ Advances in taste-masking technologies and an understanding of sensory biology are necessary to improve medication compliance and dietary pleasure^(76, 77).

Limitations of Conventional Taste Masking Techniques

Traditional taste-masking techniques like sweeteners, bitter blockers, film coatings, and physical barriers are used to make oral medications more palatable.^(71, 78) However, these methods have limitations, such as the need to add additional excipients,⁽⁷¹⁾ the effect on patient compliance and acceptance, and the inability to fully hide complex or highly bitter medications.⁽⁴⁰⁾ It's difficult to evaluate their effectiveness objectively, and they might not be compatible with all types of medications.^{(78) (55)} Therefore, new approaches like nanocarrier systems are becoming more popular as they aim to overcome these limitations without compromising the solubility or release of medications.^(56, 66)

Incomplete or Inconsistent Taste Masking Limited Effectiveness for Certain Drugs:

Traditional methods of masking the taste of prescription drugs, like mixing them with food or drinks, are not always successful and may not totally mask the unpleasant taste of some medications.^{(66) (79)} These methods depend on the specific formulation and active pharmaceutical ingredient (API) used.^{(80) (39)} Even though recent advancements in taste-masking technology, like cyclodextrins and supramolecular agents, have shown promise, each medication still requires careful selection and optimization.^(81, 82) The masking technique needs to be customized for the properties of the drug in order to be universally effective.^(55, 66, 71)

Results and Discussion

The degree to which oral medications are well tolerated has a significant effect on patient adherence, especially for younger and older patients. Traditional taste-masking techniques are often inadequate for complex active medicinal chemicals. Innovative technologies like nanotechnology-based approaches aim to increase patient compliance and palatability by encapsulating drugs.

Future Directions and Tailored Approaches

The study emphasizes the need for a tailored flavor masking approach that considers the unique characteristics of each medication as well as the patient's taste preferences. Further research is needed to optimize carrier materials, drug-to-carrier ratios, and flavoring agents. The importance of creating palatable drug formulations is underscored by the trend toward patient empowerment and collaborative decision-making.

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