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Antihypertensive Drugs and Taste Dysfunction: A Comprehensive Review

Dr. Reema Manoj[1], Dr. Mandavi Waghmare[2], Dr.Purva S. Gaikwad[3], Dr Amalsadi Mohammadzaid Iqba[l4]

[1]Department of Oral Medicine and Radiology, D.Y. Patil, School of Dentistry, Deemed to Be University, Nerul, Navi Mumbai,400706
[2]Department of Oral Medicine and Radiology, D.Y. Patil, School of Dentistry, Deemed to Be University, Nerul, Navi Mumbai,400706
[3]Department of Oral Medicine and Radiology, D.Y. Patil, School of Dentistry, Deemed to Be University, Nerul, Navi Mumbai,400706
[4]Vaidik Dental College and Research Centre, Daman.
Corresponding Author: Dr. Reema Manoj, dr.reema28@gmail.com

ABSTRACT

Taste dysfunction represents a significant yet underrecognized adverse effect of antihypertensive pharmacotherapy, affecting patient quality of life, nutritional status, and medication adherence. According to the Physicians' Desk Reference, approximately 36% of modern antihypertensive drugs produce untoward alterations in chemosensory perception. This manuscript comprehensively reviews the anatomy and physiology of the gustatory system, the mechanisms of taste perception, and the specific taste disturbances associated with major antihypertensive drug classes, including ACE inhibitors, angiotensin II receptor blockers, calcium channel blockers, beta-blockers, and diuretics. Understanding these drug-induced alterations is essential for clinicians to optimize therapeutic regimens while minimizing adverse effects that may compromise treatment compliance. The manuscript further explores future advances in personalized pharmacotherapy, biomarker identification, and novel therapeutic strategies to mitigate drug-induced gustatory dysfunction.

KEYWORDS: Gustation, dysgeusia, antihypertensive agents, ACE inhibitors, angiotensin receptor blockers, taste buds, chemosensory dysfunction

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INTRODUCTION

Taste, or gustation, is one of the five basic senses and is central to human experience and survival. It enables individuals to distinguish nutritious from potentially toxic substances, thereby influencing feeding behavior, digestion, and overall health. The sense of taste contributes significantly to quality of life by enabling differentiation among flavors and facilitating the enjoyment of food. Beyond its hedonic role, taste serves as a critical sentinel system, with bitter taste often signaling potentially harmful substances and sweet taste indicating energy-rich nutrients. This primitive warning system has evolved to protect humans from ingesting toxins while guiding them toward nutritionally valuable food sources.

Importantly, what individuals commonly refer to as "taste" is actually "flavor"—a complex composite of gustatory, olfactory, trigeminal, and visual inputs.[2]

Retronasal olfaction plays a particularly major role in what people perceive as taste, explaining why foods seem flat during nasal congestion.[1,2] This distinction has significant clinical implications, as patient complaints about taste loss do not always reflect underlying gustatory pathology, and formal taste testing is mandatory to exclude primary olfactory or trigeminal nerve pathology.[1] The integration of multiple sensory modalities in flavor perception underscores the complexity of chemosensory disorders and the need for comprehensive diagnostic approaches when patients present with taste complaints.

DEFINITION AND CLASSIFICATION OF TASTE

Taste is defined as the sensory perception accompanying oral intake, mediated by specialized neuroepithelial receptor cells that transduce chemical stimuli into electrochemical signals. This definition encompasses the entire process from molecular detection at the receptor level to central nervous system processing and conscious perception. Understanding this definition is fundamental to appreciating how pharmacological agents can interfere with various stages of the gustatory pathway.

Taste disorders are classified as either quantitative or qualitative disturbances. Dysgeusia serves as the general terminology for any taste disorder, while parageusia refers to a qualitative impairment with triggered taste distortion, such as when bitter or metallic perception occurs with eating. Phantogeusia represents a qualitative impairment with non-triggered, persistent taste distortion, essentially a phantom taste sensation. Hypogeusia is a quantitative disturbance producing reduced taste function, whereas ageusia represents the complete absence of taste, which is relatively rare in clinical practice. These distinctions are clinically important as they guide diagnostic approaches and management strategies.

The prevalence of taste disorders ranges from 0.6% to 20%, with approximately 5% of the general population having reduced

taste function, often without awareness.[3,4] These disorders are significantly underreported and underdiagnosed, as patients rarely volunteer complaints and clinicians seldom inquire about chemosensory function. Key risk factors include aging (onset around age 60), medication use, and systemic conditions such as diabetes, renal insufficiency, hepatic disease, and neurological disorders. The high prevalence and substantial impact on quality of life underscore the need for greater clinical awareness and systematic assessment.

ANATOMY OF THE TONGUE, PAPILLAE, AND TASTE BUDS

3.1 Tongue Papillae

The tongue's dorsal surface contains four types of papillae, of which three contain taste buds. Fungiform papillae are mushroom-shaped structures distributed in the anterior two-thirds of the tongue, and each fungiform papilla contains approximately five to six taste buds.[5,6] These papillae are particularly important for salt and sour taste perception and are innervated by the chorda tympani branch of the facial nerve. Foliate papillae are located along the posterior lateral edges of the tongue and contain dozens of taste buds within their folds, contributing significantly to taste perception in the posterolateral regions. Circumvallate papillae are arranged in an inverted V-shape on the posterior third of the tongue, typically consisting of approximately nine large papillae, each containing numerous taste buds.[5,6] These are the largest papillae and are innervated by the glossopharyngeal nerve. Filiform papillae are the most numerous papillae; however, these lack taste receptors and serve mechanical functions, making the tongue surface rough for food manipulation, distributing saliva, and fulfilling somatosensory functions. The filiform papillae contribute to the texture perception of food and play a role in oral hygiene through their abrasive properties.

3.2 Taste Buds

Taste buds are clusters of fifty to one hundred specialized neuroepithelial cells embedded within the lingual epithelium and housed within the connective tissue specializations of papillae. Each taste bud is a polarized structure with a narrow apical opening called the taste pore, through which solutes in the oral cavity contact the apical membranes of taste receptor cells. This structural organization ensures that tastants dissolved in saliva can access the receptor sites efficiently. Taste buds contain four distinct cell types, each with specialized functions. Type I cells, also known as dark cells, serve glial-like supporting functions and may recognize low salt taste while being involved in neurotransmitter uptake and degradation. Type II cells, or light cells, function as receptor cells utilizing G protein-coupled receptors to detect sweet, umami, and bitter tastes, and they release ATP as neurotransmitter. Type III cells, the intermediate cells, mediate responses to sour and salty stimuli and release serotonin, GABA, and norepinephrine. Basal cells serve as progenitor cells sustaining continuous taste bud regeneration, ensuring the dynamic renewal of the gustatory epithelium.[6,7]

Taste receptor cells have a limited lifespan and are continually renewed, with a median lifespan of approximately eight to twelve days. This regenerative capacity explains why drug-induced taste disturbances may resolve upon medication cessation in some cases, though permanent damage can occur if the regenerative process is compromised. The continuous turnover of taste cells also offers potential therapeutic opportunities for promoting recovery from drug-induced damage.

3.3 Innervation

Taste buds receive afferent innervation from three cranial nerves. The facial nerve, or cranial nerve VII, through its chorda tympani branch, innervates fungiform papillae and anterior foliate papillae covering the anterior two-thirds of the tongue, while the greater superficial petrosal branch innervates taste buds of the soft palate. The glossopharyngeal nerve, or cranial nerve IX, innervates circumvallate papillae and posterior foliate papillae. The vagus nerve, or cranial nerve X, innervates taste buds of the epiglottis and esophagus via the superior laryngeal branch. These fibers converge in the nucleus tractus solitarius in the brainstem and project to the thalamus and ultimately the insula, which is considered the primary gustatory cortex.[5] This well-defined neural pathway provides multiple potential sites for pharmacological interference, from receptor binding to central processing.

TASTE MECHANISM AND TYPES OF TASTE

4.1 Transduction Mechanisms

Taste transduction involves multiple molecular mechanisms depending on the taste quality, reflecting the diverse chemical nature of tastants. Sweet, bitter, and umami tastes are detected by G protein-coupled receptors expressed on Type II cells. Tastant binding activates G proteins, leading to phospholipase C activation, increased intracellular calcium, and ATP release through CALHM1 and CALHM3 channels. This signaling cascade represents a common pathway for these three taste modalities despite their distinct receptor specificities.

Sour taste is mediated by Type III cells responding to hydrogen ions through ion channels, including the OTOP1 proton channel, which allows direct detection of acidity.

Salty taste is detected by amiloride-sensitive sodium channels and other mechanisms, allowing the organism to monitor sodium homeostasis.[5,7]

4.2 Five Basic Taste Qualities

The five basic taste qualities each serve distinct biological functions and have evolutionary significance.
Sweet taste indicates energy-rich nutrients such as sugars and carbohydrates, guiding organisms toward calorie-dense food sources.

Umami, the savory taste of amino acids found in meat broth and aged cheese, signals protein content and is essential for protein

nutrition.
Salty taste allows modulation of diet for electrolyte balance, particularly sodium homeostasis, which is crucial for nerve function and fluid balance.

Sour taste typically represents the taste of acids and serves a protective function against spoiled or fermented foods that may contain harmful bacteria.

Bitter taste signals potentially harmful substances and is typically aversive, representing a crucial defense mechanism against plant alkaloids and other toxins.

Emerging evidence suggests additional taste modalities, including oleogustus for fat taste, kokumi for heartiness and enhancing continuity, and a distinct starchy taste, expanding our understanding of gustatory perception beyond the traditional five basic tastes.

ANTIHYPERTENSIVE DRUGS AND TASTE DYSFUNCTION

Drug-induced taste disturbances represent a significant clinical problem that is often overlooked in routine clinical practice. Studies have shown that approximately 20% of taste disturbances are drug-related, with antihypertensive medications being among the most commonly implicated classes.[3,8] The mechanisms of drug-induced taste dysfunction are diverse and include direct receptor interactions, alterations in salivary composition, changes in zinc homeostasis, and central nervous system effects. Understanding these mechanisms is essential for clinicians to anticipate, recognize, and manage these adverse effects.

5.1 ACE Inhibitors

Angiotensin-converting enzyme inhibitors are among the most frequently reported antihypertensives to cause taste disturbances. Their primary mechanism involves chelation of zinc, a trace element essential for taste receptor function and saliva composition. Captopril, in particular, contains a sulfhydryl group that avidly binds zinc ions, disrupting the metalloenzymes required for taste cell maintenance and function.[8] Additionally, ACE inhibitors may directly interact with taste receptors and alter salivary composition. Clinically, these drugs can cause a long-lasting sensation of bitterness or saltiness, with sweet foods tasting salty and a diminished sense of taste termed hypogeusia. Taste disturbance is a recognized adverse effect in product labeling, and the disturbance is typically reversible upon drug cessation. The specific drugs implicated include captopril, enalapril, and lisinopril, with captopril having the highest reported incidence due to its sulfhydryl-mediated zinc chelation.[8] The reversibility suggests that the underlying mechanism does not involve permanent damage to taste receptor cells.

5.2 Angiotensin II Receptor Blockers

Angiotensin II receptor blockers can blunt taste sensitivity through mechanisms independent of zinc chelation, as studies have shown they do not significantly alter serum or salivary zinc concentrations. Instead, ARBs appear to exert direct effects on taste receptor signaling pathways, possibly through interference with G protein-coupled receptor-mediated transduction cascades. A randomized, placebo-controlled, crossover study by Tsuruoka and colleagues demonstrated that repeated dosing of candesartan (4 mg/day) and valsartan (40 mg/day) significantly worsened detection thresholds for all four basic tastes.[11] The comparable effects of both drugs suggest a class effect rather than agent-specific properties.[11,12] Taste disturbance may occur within one week of treatment initiation, though patients may take several weeks to notice the problem. The specific drugs implicated include losartan, candesartan, and valsartan, with other ARBs likely producing similar effects through shared receptor antagonism.

5.3 Calcium Channel Blockers

Calcium channel blockers may affect taste through alterations in calcium-dependent signaling pathways in taste receptor cells. Since calcium influx is fundamental to taste transduction, particularly in Type II cells where calcium release is essential for neurotransmitter exocytosis, blockade of calcium channels can disrupt this process. However, the exact mechanism remains poorly characterized. Taste disturbances are reported but are generally less prominent compared to ACE inhibitors. Non-dihydropyridine calcium channel blockers are associated with multiple oral adverse effects, including gingival hyperplasia and xerostomia, which may indirectly affect taste perception.[9,10] Diltiazem and nifedipine are most commonly implicated. The relatively lower incidence may relate to their mechanism of action, which is less directly involved in taste receptor function compared to ACE inhibitors.

5.4 Beta-Blockers

Beta-blockers may alter taste through multiple mechanisms, including direct effects on taste receptors, alterations in salivary composition, and xerostomia secondary to reduced salivation. Beta-adrenergic receptors are present on taste cells[8] and may modulate sensitivity and adaptation; their blockade can therefore interfere with normal gustatory signaling. Additionally, beta-blockade reduces salivary flow through autonomic inhibition, leading to dry mouth and consequent taste changes.[8] Taste disturbances are reported but appear less frequent than with ACE inhibitors. Propranolol is most commonly associated, though other beta-blockers may produce similar effects. The role of beta-adrenergic receptors in taste cell function is not fully understood, but evidence suggests they modulate taste sensitivity through cAMP-mediated signaling pathways.

5.5 Diuretics

Diuretics cause taste disturbances primarily through xerostomia due to fluid depletion and direct effects on taste receptors. Amiloride, a potassium-sparing diuretic, is of particular interest as it causes persistent bitter taste, likely related to its mechanism as an epithelial sodium channel blocker, which may interfere with salt taste transduction.[5,7] Hydrochlorothiazide and chlorthalidone are associated with taste changes, though these are less common. Spironolactone has also been associated with

taste disturbances, possibly related to its anti-androgenic effects or alterations in electrolyte balance. The mechanism is multifactorial and may involve both direct and indirect effects on the gustatory system, including changes in salivary electrolyte composition affecting tastant solubility and receptor activation.[13]

5.6 Antihypertensives with Minimal Taste Effects and Emerging Research

While taste dysfunction is a known side effect of some antihypertensives, the risk varies significantly by drug, dose, and duration. ACE inhibitors like lisinopril and captopril show minimal impact on taste in short-term, low-dose studies, though long-term, high-dose captopril can raise taste thresholds. Losartan has a low dysgeusia incidence (0.6%), and agents like amlodipine, atenolol-chlorthalidone, and trandolapril appear rarely implicated.

Table 1. Antihypertensive Drug Classes and Associated Taste Dysfunction

Drug Class	Examples	Proposed Mechanism in Taste Dysgeusia	Key Research Findings
ACE Inhibitors	Captopril, Enalapril, Lisinopril	Zinc chelation, bradykinin/prostaglandin pathway alteration, and direct interaction with taste receptors.	• Dysgeusia reported in 8.4% of ACE inhibitor-treated patients in one study. • Captopril has extensive clinical reports of causing dysgeusia or taste loss, particularly at higher doses and in patients with renal impairment.
Angiotensin II Receptor Blockers (ARBs)	Candesartan, Valsartan, Losartan, Eprosartan	May involve reduced taste sensitivity through subclinical effects on taste pathways, possibly independent of zinc.	• ARBs can subclinically disturb taste sensitivity (including sweet, salty, sour, bitter), suggesting a possible class effect. • A case report with eprosartan confirmed a causal link via positive rechallenge (symptoms returned when the drug was restarted).
Diuretics	Hydrochlorothiazide, Chlorthalidone, Amiloride, Spironolactone	• Xerostomia: Fluid depletion reduces salivary flow, indirectly impairing tastant transport and receptor function. • Hydrochlorothiazide/Chlorthalidone: Can alter salivary flow/composition and stimulate sodium intake. • Amiloride: Epithelial sodium channel (ENaC) blockade may interfere with salt-taste transduction, producing a persistent bitter taste. • Spironolactone: Associated with taste disturbance, possibly via its anti-androgenic effects and alterations in electrolyte balance. • Overall, the mechanism is multifactorial, involving direct and indirect effects on salivary electrolyte composition, tastant solubility, and receptor activation.	• Hydrochlorothiazide significantly increased the sodium/creatinine ratio (~50% higher) after 4 weeks, a finding that may reflect altered renal sodium handling rather than a directly observed change in salt appetite. • Amiloride caused a 39% decrease in salivary sodium and a 28% decline in NaCl recognition thresholds. • Amiloride's persistent bitter taste is attributed to ENaC blockade interfering with salt-taste transduction pathways. • Chlorthalidone- and spironolactone-associated taste disturbances are reported less frequently than with hydrochlorothiazide or amiloride, with spironolactone's effect possibly linked to its anti-androgenic and electrolyte-altering properties.
Beta-Blockers	Propranolol, Labetalol	Direct action on peripheral taste receptors and possible alterations to salivary flow.	• Clinical reports document complete hypogeusia (reduced taste sensitivity) in patients receiving propranolol therapy. • Taste loss reported to be dose-dependent and gradually reversible upon drug withdrawal. • Topical application of propranolol to the tongue was rated as primarily bitter by study participants. • Propranolol-induced taste changes have been associated with anorexia and subsequent weight loss, which is particularly concerning in geriatric

Drug Class	Examples	Proposed Mechanism in Taste Dysgeusia	Key Research Findings
			populations.
Calcium Channel Blockers	Diltiazem	Direct interaction with peripheral taste receptors, potentially altering membrane ion channel activity.	• Clinical case reports describe taste distortion (dysgeusia) in patients treated with labetalol. • The distorted taste is often characterized as bitter or unpleasant. • Topical application of labetalol to the tongue was rated as primarily bitter. • Taste disturbances typically resolve upon discontinuation of the drug.

CLINICAL IMPLICATIONS AND MANAGEMENT

6.1 Impact on Quality of Life and Compliance

Drug-induced taste disturbances have clinical consequences beyond sensory alteration. Decreased food intake can precipitate nutritional deficiencies and weight loss, especially in elderly patients. Depression often accompanies altered taste, as eating is central to pleasure and social engagement, while reduced quality of life affects physical and emotional well-being. Most critically, medication non-adherence is a major concern, as patients may discontinue antihypertensives without consulting providers, leading to uncontrolled hypertension and increased cardiovascular risk. This underscores the need for clinicians to proactively inquire about taste changes and address them appropriately.

6.2 Management Strategies

Optimal management requires systematic differential diagnosis excluding age, smoking, infections, diabetes, liver/renal disease, and zinc deficiency. A thorough medication review should identify all offending agents. Drug substitution within or across antihypertensive classes may resolve the issue while maintaining control. For xerostomia, sipping water and adjusting meal seasoning help. Patient education on reversibility encourages adherence. Zinc supplementation lacks strong evidence for drug-induced taste disorders.[14]

CONCLUSION

Antihypertensive-induced taste dysfunction impairs quality of life, nutrition, and medication adherence, with ACE inhibitors most commonly implicated. Management involves differential diagnosis, drug substitution, symptomatic care, and education. Future research should employ pharmacogenomic approaches to identify genetic polymorphisms that predispose certain individuals to drug-induced dysgeusia, thereby enabling personalized antihypertensive therapy selection.

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