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Faculty of Pharmacy - Tanta University

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The American Gastroenterological Association (AGA) updates clinical practice on potassium-competitive acid blockers (P-CAB) use

Last November, the American Gastroenterological Association (AGA) issued a clinical practice update to summarize the available evidence and offer expert best practice advice on the integration of potassium-competitive acid blockers (P-CABs) in the clinical management of foregut disorders, specifically gastroesophageal reflux disease, *Helicobacter pylori* infection, and peptic ulcer disease.

What are P-CABs?

P-CABs, a class of acid suppressants, were developed in the 1980s. The first drug, revaprazan (Revanex), was discarded due to hepatotoxicity and the second was not superior to esomeprazole. The second, vonoprazan fumarate, was introduced in Japan in 2015 and gained popularity due to its rapid onset, long duration, and potent acid suppression compared to traditional proton-pump inhibitors (PPIs). In November 2023, the FDA approved vonoprazan as a therapy for erosive gastroesophageal reflux disease.

Mechanism of action:

P-CABs suppress gastric acid secretion by binding to H+, K+-ATPase in the gastric parietal cell, blocking potassium ion access. Unlike PPIs, they are acid-stable, do not require pre-meal dosing, and do not require conversion to an active form for pharmacologic effect facilitating a more rapid onset of action. P-CABs can bind to proton pumps for longer periods, allowing for more prolonged gastric acid inhibition than PPIs.

They are not metabolized by CYP2C19, reducing genetic polymorphisms that impact PPI metabolism, resulting in variability in pharmacologic and therapeutic outcomes. Differences between both groups are illustrated &summarized in the following table:

	P-CAB Class	PPI Class
Examples of Medications	Fexuprazan, keverprazan, revaprazan, tegoprazan, vonoprazan	Dexlansoprazole, esomeprazole, lansoprazole, omeprazole, pantoprazole, rabeprazole
Prodrug	No	Yes
Acid Stability	Yes	No
Inhibition and Binding	Reversible, ionic	Irreversible, covalent
Maximal Acid Suppression After Dosing	1 day (vonoprazan)	3-5 days
Half-Life	6-9 hours (vonoprazan)	1-2 hours
Significantly Affected by CYP2C19 Polymorphism	No	Yes
Optimal Dosing Administration	Independent of mealtimes (before or after meals)	30-60 minutes prior to mealtimes (for most PPIs)

AGA best practice advice on the integration of (P-CABs) :

- The expert review suggests that P-CABs should be used in place of PPIs in eradication regimens for most patients with H pylori infection. However, due to nonclinical factors like cost, difficulty in obtaining medication, and fewer long-term safety data, they should not be used as initial therapy for acid-related conditions.
- P-CABs should not be used as first-line therapy for uninvestigated heartburn, nonerosive reflux, milder esophagitis, or peptic ulcer. Instead, they may be used in patients with documented acid-related reflux.
- P-CABs' rapid and potent acid inhibition may be useful in patients with bleeding gastro-duodenal ulcers and high-risk stigmata.

References:

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Esketamine .. The first approved monotherapy for resistant depression

Esketamine nasal spray (Spravato CIII; Janssen Pharmaceuticals) has received FDA approval in 2025 as the first monotherapy for adults with treatment-resistant depression (TRD) who have not responded adequately to at least two oral antidepressants. This groundbreaking monotherapy demonstrated significant improvements in depressive symptoms as quickly as 24 hours after administration, meeting its primary endpoint at the 4-week mark.

Spravato® (esketamine) CIII nasal spray

TRD, which affects about 30% of major depressive disorder (MDD) cases, is diagnosed in patients who fail to respond to two oral antidepressants, significantly impacting quality of life and imposing substantial financial burdens. Traditional treatment approaches often require patients to try multiple medications, with each attempt taking 4-6 weeks to assess efficacy. Notably, by the third oral antidepressant trial, approximately 86% of patients still do not achieve remission.

Initially approved by the FDA in 2019 as a combination therapy with oral antidepressants for TRD, esketamine is administered as a nasal spray in certified healthcare settings. It functions as a non-selective, non-competitive antagonist of the N-methyl-D-aspartate receptor, targeting glutamate pathways in the brain. However, the precise mechanism by which it exerts its antidepressant effects remains unknown.

The 2025 monotherapy approval is based on a randomized, double-blind, multicenter, placebo-controlled study that demonstrated esketamine's superior efficacy compared to placebo. The trial showed that 22.5% of patients receiving esketamine achieved remission by week 4, compared to 7.6% in the placebo group.

Safety and Tolerability

The safety profile of esketamine has been extensively studied, with most adverse effects being transient and manageable. Common side effects include dizziness, dissociation, nausea, and increased blood pressure, which typically resolve within a few hours post-administration. Long-term studies have indicated that esketamine does not lead to severe bladder pathology or cognitive impairments when used according to guidelines, although some concerns about urinary tract symptoms have been noted. The need for monitoring after administration is crucial to manage these side effects effectively.

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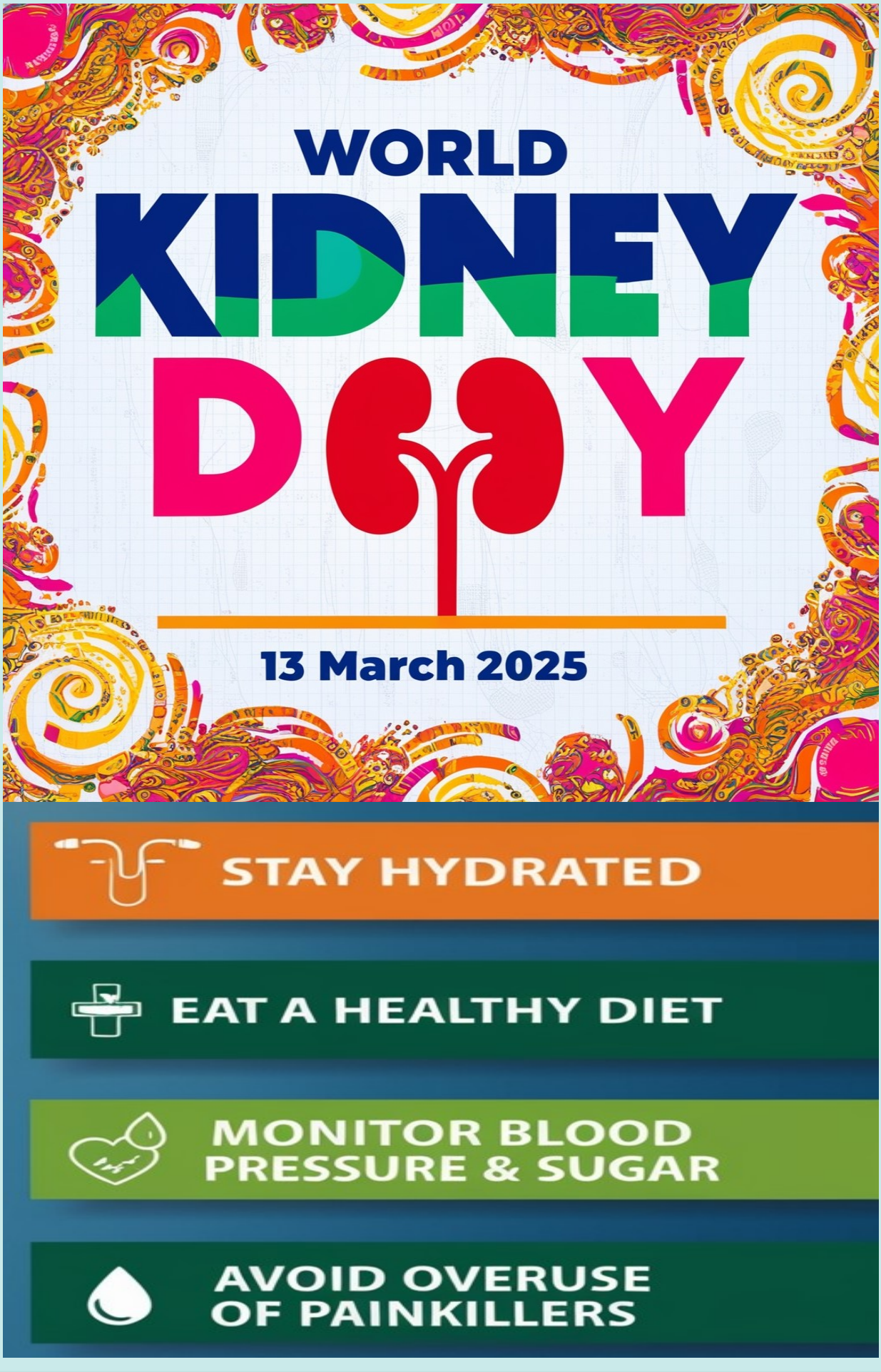
WORLD
KIDNEY
DAY
13 March 2025
STAY HYDRATED
EAT A HEALTHY DIET
MONITOR BLOOD PRESSURE & SUGAR
AVOID OVERUSE OF PAINKILLERS

Refresh your knowledge.. bee venom therapeutic applications

Bee venom, also known as apitoxin, is a clear, colorless liquid produced by worker honeybees (*Apis mellifera*). It is primarily used as a defensive mechanism against threats to the hive, such as predators. Over 80% of bee venom is composed of water, and only about 0.1 µg of dry venom can be extracted from a single bee.

Composition:

Bee venom has a complex structure consisting of peptides: melittin, apamin, mast cell degranulating peptides, ado-lapin, and proteins with enzymatic properties: including phospholipase A2, and hyaluronidase. These molecules exhibit antimicrobial, anti-inflammatory, and analgesic properties, which lead to investigations into venom's potential therapeutic application for conditions such as arthritis, gout, multiple sclerosis, chronic pain, and skin disorders. In addition, bee venom contains many low molecular mass compounds, such as sugars, amino acids, phospholipids, and pheromones.

Various factors such as bee age, seasonal changes, and the strain of honeybee have an impact on the quantitative composition of bee venom. For example, melittin content rises steadily from eclosion until reaching the peak at four weeks of age, after which it declines gradually. Additionally, melittin levels reach to peak in March and May, then decrease to their lowest levels in January.

What is melittin?

Melittin, the primary component of bee venom representing 40-60% of the dry weight. It is synthesized by secretory cells within the bee venom glands as an inactive precursor known as prepromelittin. The activation of this 70 amino acid-long precursor is a multistep process ended with, the C-terminal glutamine-glycine dipeptide. Finally, the C-terminal glutamine-glycine dipeptide is enzymatically converted to a terminal glutamine-amide to give the native 26-residue peptide amide melittin. In addition, it has been shown to suppress inflammatory pathways and reduce inflammatory markers, such as tumor necrosis factor-alpha (TNF-α) and interleukin 1 beta (IL-1β).

Therapeutic applications:

Bee venom has numerous biological activities, including analgesic, anti-cancer, anti-asthmatic, antioxidant, anti-aging, anti-atherosclerotic, anti-diabetic, hepatoprotective, antiviral, neuroprotective, and anti-rheumatoid arthritis. It's used in the cosmetic industry and has shown efficacy in treating chronic and autoimmune diseases, managing pain, and improving quality of life.

Treatment techniques

There are numerous BV-based treatments available including:-

- **Live bee sting therapy,** which involves the direct injection of BV into human body via live bee stings which must be done through a trained medical professional. It is likely to be safe for most people. In some cases this technique has a chance of causing undesirable side effects such as redness and swelling at the sting site.
- **BV acupuncture (BVA):** It is a pharmacopuncture treatment that uses the diluted BV to treat various diseases like rheumatoid arthritis, chronic low back pain, acne, diabetes, Parkinson's, Alzheimer's, and asthma. This technique involves injecting BV diluted with saline into specific acupoints and is used in traditional, complementary, and alternative medicine. It's originated from beekeepers' experiences with rheumatism and joint pain.

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Vision

The vision of Tanta University DPIC is to improve national healthcare service through provision of evidence-based, unbiased, patient oriented drug information services & adverse drug reporting system.

Mission

* Responding to drug inquiries related to the use of the drug and providing the health care professionals and patients with drug information related to the patient's care to achieve the optimal use of the drug in addition to the provision of other toxicological managing information.
* Educational activities to support the rational optimal use of drugs as well, supporting research activities.
* Continuous medical education and training courses in various fields of pharmacy for students, undergraduates, postgraduate students, and researchers.
* Issuing a Drug Information Bulletin periodically to take a look at medical & pharmaceutical news.
* Supporting the National Pharmaceutical Vigilance Program by following up and monitoring side effects and problems related to use of pharmaceutical preparations within regional hospitals.
* Contributing to the establishment of various treatment protocols and prescription booklet services in regional hospitals.

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