Clinician Reviews®

Roots, Fruits, Shoots—and Drugs

For centuries, humans have sought relief from disease and pain by using bark, seeds, and other parts of plants. Did you know that some of these folk remedies are the source of today's medical armamentarium?

Match the originating organism to its drug isolate:

a. Etoposide b. Morphine c. Artemisinin d. Paclitaxel

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1. An annual flowering plant—originating in ancient Egypt, Mesopotamia, and Persia—the poppy is valued for its edible seeds, ornamental flowers, and medicinal properties. The first known written reference to the poppy appeared in 4000 BC in Sumerian text. In the medieval period, Avicenna described the poppy under the entry *Afion* of his medical encyclopedia *Canon of Medicine.* In the traditional system of medicine, the air-dried milky latex of unripe seed capsules is a remedy for a number of diseases and disorders.

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2. The Pacific yew grows as a shrubby understory tree in a number of coniferous forests of the Pacific Northwest and northern Rocky Mountains. Tonics made from Pacific yew were used medicinally by many Native American peoples. Although the seeds are poisonous, the fleshy portions surrounding them were sometimes eaten.

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3. Native to the United States, mayapple occurs in damp, open woods as dense mats of foliage arising from a single rhizome. Although the leaves, roots, and seeds are poisonous if ingested in large quantities, the roots were used as an emetic, cathartic, and antihelminthic by Native Americans and early settlers.

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4. Sweet wormwood—also known as *sweet annie* and *sweet sagewort*—is an herb native to China, where it is called *qinghao,* meaning "from the green herb." Its intensive aromatic scent is characteristic. Steeped in hot water according to Chinese tradition, the herb has been employed to treat fevers for more than 2,000 years.

ANSWERS

Discussion: Opiates, present in the poppy (*Papaver somniferum*), were widely used by 18th-century physicians to reduce spasm, pain, and excitement, as well as alter behavior, induce sleep, and reduce anxiety.

Morphine, the first active alkaloid purified from a plant source, was discovered by Friedrich Sertürner, a 21-year-old pharmacist's apprentice. He reported his discovery of a sleep-inducing molecule in letters to the editor of the *Trommsdorffs Journal der Pharmacie* in 1805. Sertürner named the substance *Morphium* after the Greek god of sleep and dreams.

Morphine sulfate is an opioid agonist indicated for the management of pain not responsive to nonnarcotic analgesics. It can be administered orally, intravenously, rectally, and subcutaneously, as well as through spinal injection (eg, epidural) or inhalation. Highly addictive, the drug causes severe adverse effects that can lead to respiratory and cardiac depression, cardiac arrest, and ultimately death. Nonopioid therapy is preferred for chronic pain outside active cancer, palliative, and end-of-life care.

Related Articles

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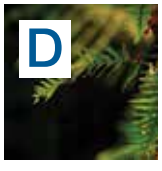

Discussion: In 1962, Arthur S. Barclay of the USDA collected bark from a single Pacific yew tree (*Taxus brevifolia*) in a forest in Washington State as part of a 4-month trip to collect material from more than 200 different species. In 1964, a cellular assay of one of the bark samples was found to have antineoplastic properties.

Taxomyces andreanae, a fungal endophyte, was isolated from the inner bark of the Pacific yew; when cultured, it produced **paclitaxel** and related compounds. From 1967 to 1993, almost all paclitaxel was produced from the bark of trees harvested from the wild, killing the trees in the process. Today, paclitaxel is derived as a semisynthetic product from related *Taxus* species.

Paclitaxel is in a class of medications called *antimicrotubule agents.* As an injection (with albumin), it is used for treatment-resistant breast cancer. It is also used in combination with other chemotherapy medications to treat non-small cell lung cancer. It works by slowing or stopping the growth and spread of cancer cells.

Related Articles

Oeffinger KC, Fontham ETH, Etzioni R, et al. Breast cancer screening for women at average risk: 2015 guideline update from the American Cancer Society. *JAMA.* 2015;314(15):1599-1614.

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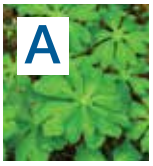

Discussion: The rhizome of the mayapple (*Podophyllum peltatum*) is the source of podophyllotoxin, which is highly toxic if consumed. Mayapple may be used topically to remove certain kinds of warts but is better known as the source of **etoposide.**

Etoposide injection is a chemotherapy medication used in combination with other medications for treatment-resistant testicular cancer, small cell lung cancer, and certain other cancers. This product was granted FDA approval in 1983 and is on the World Health Organization's List of Essential Medicines.

Related Articles

Etopophos (etoposide phosphate) [package insert]. Deerfield, IL: Baxter Healthcare Corporation; 2019. https://packageinserts.bms.com/pi/pi_etopophos.pdf. Updated May 2019. Accessed August 19, 2019.

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Discussion: **Artemisinin,** an antimalarial lactone, was first isolated from sweet wormwood (*Artemisia annua*) by Tu Youyou, a Chinese scientist, who was corecipient of the 2015 Nobel Prize in Medicine for her discoveries concerning this novel therapy against malaria.

Artemisinin and its semisynthetic derivatives (arteether, artemether, and artesunate) are known for their ability to reduce the number of *Plasmodium falciparum* parasites in the blood of patients with malaria. Additional reported pharmacologic activities include cytotoxicity against cancer cells and antibacterial, antifungal, and other types of helminthic infections.

Use of artemisinin as monotherapy is explicitly discouraged by the World Health Organization, because of increasing resistance to the drug. Artemisinin-combination therapies (ACTs) are still the best available treatment worldwide for acute uncomplicated *P falciparum* malaria,

ANSWERS cont'd

despite reports of increased resistance to ACTs as well in certain settings. Because of the potential for teratogenicity, use in women during the first trimester of pregnancy is to be avoided. **CR**

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Coartem (artemether-lumefantrine) [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corp; 2019. www.pharma.us.novartis.com/sites/www.pharma.us.novartis.com/files/coartem.pdf. Updated August 2019. Accessed August 19, 2019.

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