Biološki učinci kapsaicina

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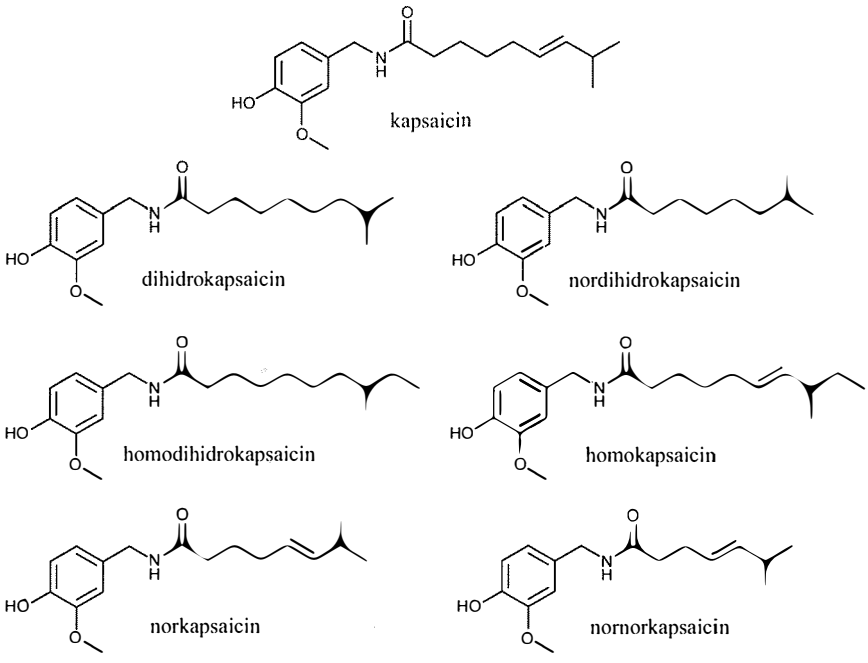
Uvod

Kapsaicinoidi su skupina srodnih alkaloida koji su odgovorni za ljuti okus paprike. U kapsaicinoide spadaju kapsaicin, dihidrokapsaicin, nordihidrokapsaicin, homodihidrokapsaicin, homokapsaicin, norkapsaicin i nornorkapsaicin (slika 1.) (1). Svi su amidi vanililamina i karboksilnih kiselina s 8–11 ugljikovih atoma, sa ili bez dvostruke veze. Kapsaicin (*trans*-8-metil-*N*-vanilil-6-nonenamid) je najviše zastupljen i najviše proučavan kapsaicinoid. Derivat je homovanilinske kiseline. Promjenama u kiselinskom i aromatskom dijelu molekule dobiveni su derivati različitog stupnja ljutine (2).

Paprika pripada porodici Solanaceae, rodu *Capsicum*, u kojem se nalazi 25 divljih i 5 domesticiranih vrsta (*C. annuum*, *C. baccatum*, *C. chinense*, *C. frutescens* i *C. pubescens*) (slika 2.). Najljuća među njima je *C. chinense*. Zbog posebnog okusa, privlačne boje i visokog sadržaja antioksidansa (vitamina C i E te karotenoida) paprika je izuzetno cijenjena prehrambena namirnica, a koristila se i u narodnoj medicini kao lijek (1). U ovom radu ukratko su opisani najvažniji biološki učinci kapsaicina i njegovih derivata te njihova primjena u suvremenoj terapiji.

Biološki učinci kapsaicina

Znanstvena istraživanja potvrdila su analgetsko (3–5), antioksidativno (6, 7), protuupalno (8, 9), anoreksično (10, 11) i antitumorsko djelovanje kapsaicina (1). Analgetsko i protuupalno djelovanje kapsaicina (12) objašnjava se agonističkim djelovanjem na vaniloidne receptore TRPV1 (*transient receptor potential vanilloid type-1*) (13). Vezanjem kapsaicina na te receptore pokreće se cijeli niz zbivanja koja dovode do smanjenja koncentracije supstance P i desensibilizacije senzoričkih neurona, čime se postiže analgetski učinak (14, 15). Kapsaicin ili

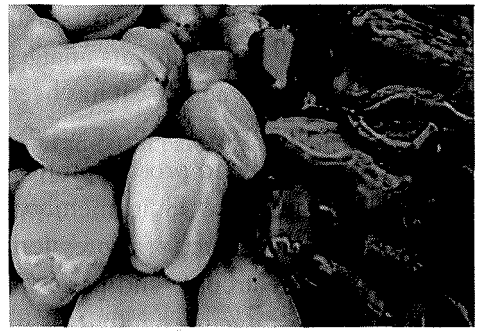


Slika 1. ▶ Strukturne formule kapsaicina i srodnih kapsaicinoida.

ekstrakt ljute paprike upotrebljava se topički u obliku krema, losiona ili flastera. Mnoga istraživanja usmjerena su na sintezu analoga kapsaicina s jačim analgetskim (16–18), antioksidativnim (19) ili protuupalnim djelovanjem (20).

Postoje mnogobrojni dokazi o antitumorskom djelovanju kapsaicina na staničnim kulturama *in vitro* i na životinjskim modelima *in vivo* (1, 21–23). Antitumorsko djelovanje kapsaicina temelji se na pro-apoptotičkom djelovanju koje je također posljedica vezanja na TRPV1 receptore. Naime, TRPV1 receptori su eksprimirani na većini tumorskih stanica, npr. na stanicama karcinoma dojke (MCF-7 i BT-20) (24, 25), prostate (LNCaP i PC-3) (26), adenokarcinoma kolona te karcinoma pankreasa (27). Međutim, mehanizam kojim kapsaicin uzrokuje apoptozu u tumorskim stanicama nije tako jednostavan niti u potpunosti poznat, a uključuje porast koncentracije iona kalcija u stanici, stvaranje reaktivnih kisikovih specija (ROS), kidanje membrane mitohondrija te aktivaciju nekih transkripcijskih faktora (28–30). Povezanost između kapsaicina i stvaranja ROS-a također je vrlo kompleksna (31). Nadalje, kapsaicin zaustavlja stanični ciklus inhibicijom ciklina i ciklin-ovisnih kinaza (CDKs, *cyclin-dependent kinases*). Tako su Chen i suradnici dokazali da kapsaicin sprječava proliferaciju stanične linije 5637 karcinoma mjehura inhibicijom nekoliko ciklin-ovisnih

ciklaza (CDK2, CDK4 i CDK6) (32). Osim toga, kapsaicin inhibira protein toplinskog šoka (*heat shock protein* 90, Hsp90) (33) te inducira fosforilaciju tumor-supresorskog proteina p53, koji, između ostalog, posreduje u staničnom odgovoru na oštećenja DNA i apoptozi (34). Zbog svega iznesenog, kapsaicin je poslužio kao polazni spoj za razvoj novih potencijalnih citostatika (35–38). Opisan je i sinergistički učinak kapsaicina s antitumorskim (5-fluorouracil, docetaxel) (39, 40) i drugim ljekovitim tvarima (resveratol, pirarubicin, brassinin) (23).



Slika 2. ▶ Paprika – raznolikost boja i oblika.

I na kraju, da bi se objasnilo anoreksičko djelovanje kapsaicina ispitivan je učinak kapsaicina na oreksigene i anoreksigene peptide u hipotalamusu štakora. Dokazano je da kapsaicin smanjuje koncentraciju neuropeptida Y (NPY) u arkuatnoj i paraventrikularnoj jezgri hipotalamusa, a povećava koncentraciju kolecistokinina (CCK) (11). Time je primjena različitih pripravaka za mršavljenje na bazi paprike i znanstveno opravdana. U ljekarnama su dostupne kapsule s ekstraktom paprike, namijenjene za mršavljenje, točnije za brže sagorijevanje masnoća (ubrzanje metabolizam). Sadrže i ekstrakt crnog papra (*Piper nigrum*), kofein i niacin (vitamin B3). Međutim, uz uzimanje pripravaka za mršavljenje treba promijeniti i prehrambene i životne navike, tj. uvesti zdraviju prehranu, ravnomjerne obroke i povećati fizičku aktivnost.

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Biological effects of capsaicin

B. Zorc

Abstract Capsaicinoids (capsaicin, dihydrocapsaicin, nordihydrocapsaicin, homodihydrocapsaicin, homocapsaicin, norcapsaicin and nornorcapsaicin) are alkaloids present in *Capsicum* species responsible for their pungency. In addition, peppers are rich sources of carotenoids, vitamins C and E, and as such, have a wide application in food, medicine and pharmacy.

Capsaicin is the most important and the most abundant capsaicinoid. It has been extensively studied for its analgesic, anti-inflammatory, antioxidant, anorexic and anticancer activity. It has been shown that capsaicin alter expression of several genes involved in cancer survival, growth arrest, angiogenesis and metastasis. Its analgesic and pro-apoptotic activity is mediated by transient receptor potential subfamily vanilloid member 1 receptor (TRPV1), while anti-obesity activity is a consequence of expressional changes of neuropeptide Y and cholecystokinin in the arcuate and paraventricular nuclei of hypothalamus. On the other hand, the anticancer activity is mediated through the direct interaction of capsaicin with key signaling molecules of the cytoplasmic, mitochondrial and metabolic survival pathways. Various patches, plasters, creams and capsules with capsaicin or chili pepper extracts are available in the pharmaceutical market.

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