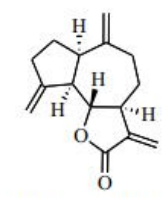
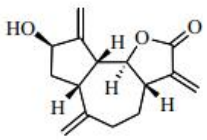
云木香研究进展

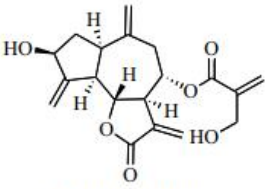
云木香（*Saussurea lappa*）为菊科风毛菊属植物。在我国云南、重庆、四川、广西、贵州等地均有分布。云木香是一种多年生高大草本植物，有 1-2 米高，茎直立[1]。其根粗壮，长约 60 厘米，且具有特征气味。其茎是纤维状的，长约 1m。花为黑色至略带紫色，并排列在顶生和腋生的簇中。花的头是圆形的，无茎，坚硬，直径约 3-4 厘米[2]。云木香干燥的根可药用。其干燥的根长 8-12 厘米，直径 1-3 厘米，味微苦，颜色为灰色至黄色[3]。根和根茎通常被用于治疗炎症，发烧，咳嗽，哮喘，头痛，牙痛，皮肤病，风湿病，瘫痪等疾病[4]，也可用于治疗月经不调、腹痛和癌症等[5]。

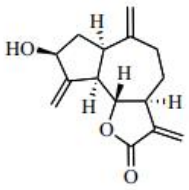
1. 植物化学

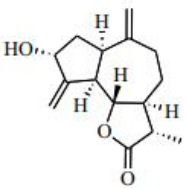
目前已从云木香根中分离出一系列生物活性成分，包括倍半萜类、黄酮类、木脂素类、植物甾醇生物碱类、萜烯蒽醌类等，而倍半萜类化合物是其主要的活性成分，参与了多种药理作用[6]。根据碳环骨架，倍半萜大致可分为三类：愈创木烷型、桉叶烷型和吉马烷型。截至目前，已从云木香的根中分离得到的倍半萜类化合物如图 1[6]。

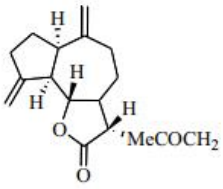

Dehydrocostus Lactone (1)

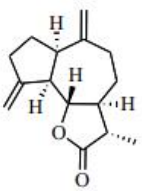

3-Epizaluzanin C (2)

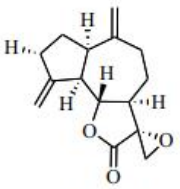

Cynaropicrin (3)

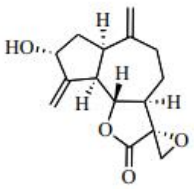

Zaluzanin C (4)

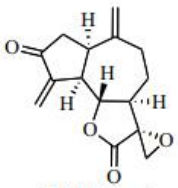

11b,13-Dihydro-3-epizaluzanin C (5)

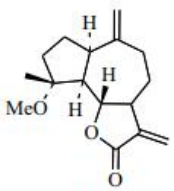

Lappalone (6)

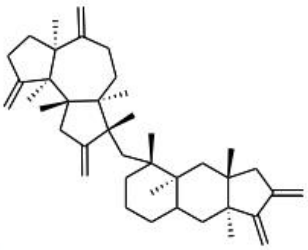

Dihydrodehydrocostuslactone (7)

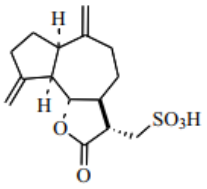

11,13-Epoxydehydrocostuslactone (8)


11,13-Epoxyisozaluzanin C (9)

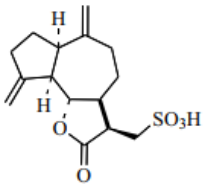

11,13-Epoxy-3-ketodehydrocostuslactone (10)


4-Methoxy DehydroCostuslactone (11)

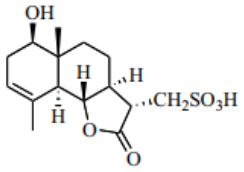

Lappadilactone (12)



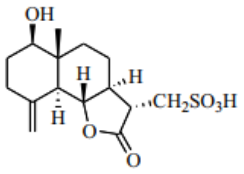
Sulfocostunolide A (13)



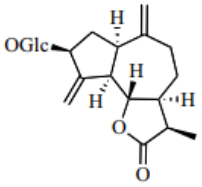
Sulfocostunloide B (14)



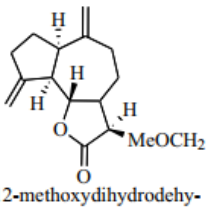
13-Sulfodihydrosantamarine (15)



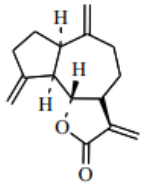
13-Sulfodihydroreynosin (16)



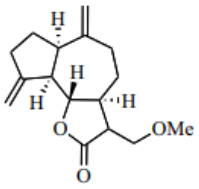
11,13 dihdroglucozanin C (17)



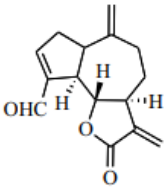
12-methoxydihydrodehydrocostuslactone (18)



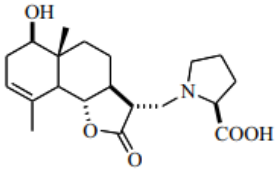
Saussureal (19)



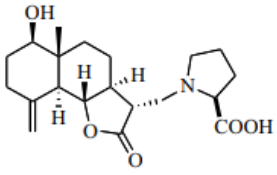
13 Methoxydihydrodehydrocostuslactone (20)



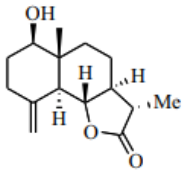
Isodehydrocostuslactone 15-aldehyde (21)



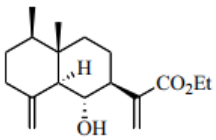
Saussureamine D (22)



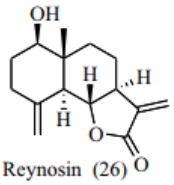
Saussureamine E (23)



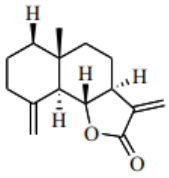
11β,13-Dihydroreynosin (24)



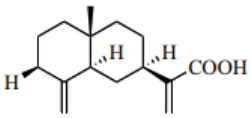
1β,6α-Dihydroxycostic acid ethyl ester (25)



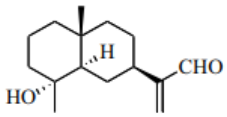
Reynosin (26)



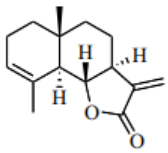
β-cyclocostunolide (27)



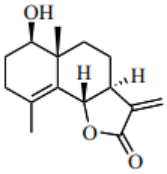
β-costic acid (28)



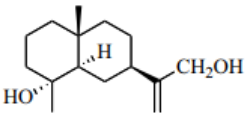
4β-hydroxyeudesm-11 (13)-en-12-al (31)



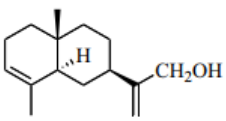
α-cyclocostunolide (29)



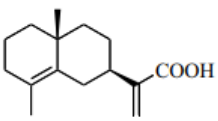
Magnolialide (30)



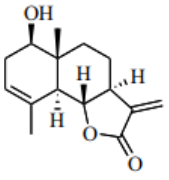
4α-hydroxy-4β-methyldihydrcostol (32)



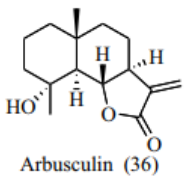
α-costol (33)



Isocostic acid (34)



Santamarine (35)



Arbusculin (36)

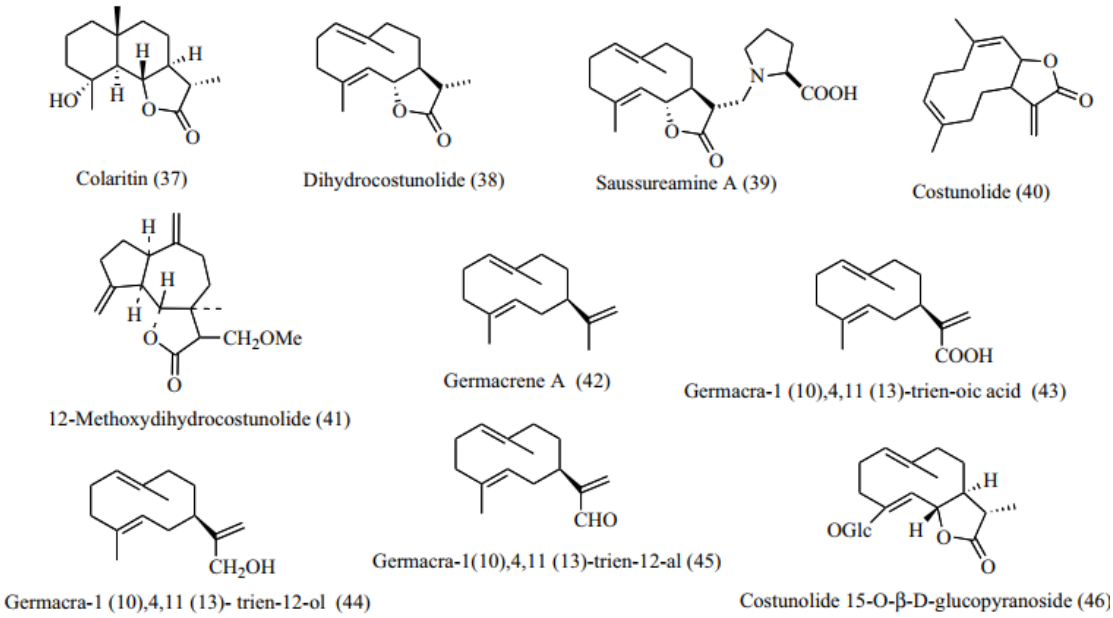


图 1 从云木香中分离得到的多种倍半萜类化合物

2. 主要药理活性

2.1 抗肿瘤

从云木香中分离得到的木香烃内酯（Costunolide, CT）可通过选择性抑制血管内皮生长因子（VEGF）诱导的内皮细胞增殖来发挥抗血管生成作用。此外，还发现（CT）可抑制 VEGF 诱导的人脐静脉内皮细胞趋化性，IC50 为 3.4 μM。在小鼠角膜微囊化验的体内方法中，当评估该化合物被 VEGF 诱导的血管新生时，剂量为 100mg / kg / day 时，小鼠角膜的新血管形成受到了显着抑制，这表明其具有抗血管生成作用。还通过信号传导途径证明了对 VEGFR KDR / Flk-1 的抑制作用[7]。在活性导向下的对云木香根的甲醇提取物进行分离纯化，得到 betulinic acid, betulinic acid methyl ester, dehydrocostus lactone 和 mokko lactone。通过蛋白酪氨酸磷酸酶（PTP1B）的体外抑制试验，证明该 4 种化合物显示出对酪氨酸磷酸酶抑制剂的有效活性[8]。

2.2 抗炎

研究了云木香根乙醇提取物对小鼠和大鼠急性和慢性炎症反应的影响，并对角叉菜胶（50-200mg/kg）引起的足肿胀有显著的抑制作用。此外，它还能防止角叉菜胶诱发的腹膜炎中炎性细胞的积聚[9]。Costunolide 对 LPS 刺激的 RAW 264.7 细胞中白介素-1β（1L-1β）的蛋白质和 mRNA 表达具有明显的抑制作用。 1st-

1ol 启动子的转录活性也被木香酚抑制。 costunolide 也抑制 1L-1β 启动子的转录活性，同时也能抑制 AP-1 转录因子的活性、丝裂原活化蛋白激酶（MAPKS）、SAPK/JNK 和 p38map 激酶的磷酸化。所有这些因素都表明，Costunolide 通过阻断 LPS 刺激的 RAW 264.7 细胞中 MAPKS 的激活而抑制 1L-1β 基因表达，从而显示出抗炎活性[10]。

2.3 胃保护与胃功能

从云木香根的甲醇提取物中分离出的 Costunolide, dehydrocostus lactone, saussureamines A, B, C 在 5-10 mg/kg 的剂量范围内表现出显著的胃保护作用。同时 saussureamines A 对小鼠水浸应激所致的胃粘膜损伤也有显著的抑制作用[11]。

参考文献：

[1] Madhuri K, Elango K, Ponnusankar S. *Saussurea lappa* (Kuth root): Review of its traditional uses, phytochemistry, and pharmacology[J]. Orient Pharm Exp Med. 2012, 12(1): 1-9.

[2]《中国植物志》[M]. 1999, 12: 8-10.

[3]《中国药典》[M]. 2020.一部. 63.

[4] Shah NC. Herbal folk medicines in Northern India[J]. J Ethnopharmacol. 1982, 6(3): 293-301.

[5] Ko SG, Kim HP, Jin DH, et al. *Saussurea lappa* induces G2-growth arrest and apoptosis in AGS gastric cancer cells[J]. Cancer Lett. 2005, 220(1): 11-9.

[6] Reyaz Hassan1, Mubashir Hussain Masoodi. *Saussurea lappa*: A Comprehensive Review on its Pharmacological Activity and Phytochemistry[J]. Current Traditional Medicine. 2020, 6(1): 13-23.

[7] Jeong S-J, Itokawa T, Shibuya M, et al. Costunolide, a sesquiterpene lactone from *Saussurea lappa*, inhibits the VEGFR KDR/Flk-1 signaling pathway[J]. Cancer Lett. 2002, 187(1-2): 129-33.

[8] Choi JY, Na M, Hyun Hwang I, et al. Isolation of betulinic acid, its methyl ester and guaiane sesquiterpenoids with protein tyrosine phosphatase 1B inhibitory activity from the roots of *Saussurea lappa* C.B.Clarke[J]. Molecules. 2009, 14(1): 266-72.

[9] Gokhale AB, Damre AS, Kulkami KR, Saraf MN. Preliminary evaluation of anti-inflammatory and antiarthritic activity of S. *lappa*, A. speciosa and A. aspera[J]. Phytomedicine. 2002, 9(5): 433-7.

[10] Kang JS, Yoon YD, Lee KH, Park SK, Kim HM. Costunolide inhibits interleukin-1β expression by down-regulation of AP-1 and MAPK activity in LPSstimulated RAW 264.7 cells[J]. Biochem Biophys Res Commun. 2004, 313(1): 171-7.

[11] Matsuda H, Kageura T, Inoue Y, et al. Absolute stereostructures and syntheses of saussureamines A, B, C, D and E, amino acid-sesquiterpene conjugates with gastroprotective effect, from the roots of *Saussurea lappa*[J]. Tetrahedron. 2000, 56(39): 7763-77.