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评述与展望

Review and Progress

印斯榄仁木(*Terminalia arjuna* L.)的植物化学和药理潜力

Z. M. Halleys Khan , Hossain Md. Faruquee , Md. Munan Shaik
Department of Biotechnology and Genetic Engineering, Islamic University, Kushtia-7003, Bangladesh
通讯作者: munanbt2004@gmail.com; mmshaik@btge.iu.ac.bd 作者
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摘　要　自古以来，药用植物就作为一种主要的药物资源用来治疗人类疾病。在孟加拉国，印斯榄仁木是一种广泛使用的药用植物，在 Ayurveda、Sidda 和 Unani 当地医疗系统中使用。据报道，这种植物含有有效成分包括阿江榄仁酸、没食子酸、榄仁酸、邻苯二酚、β-谷甾醇、钙、镁、锌、铜等，研究证明这些成分具有有效的药理学作用，比如抗菌、抗癌、抗糖尿病、祛痘、驱虫、抗炎、抗胆碱酯酶、抗氧化、平喘以及伤口愈合、护心和杀虫活性。它被认为是一个理想的药剂用于治疗癌症、冠心病、高血压和缺血性心肌病。本综述力图详细介绍有关印斯榄仁木最近的化学成分研究和药理学研究。

关键词　印斯榄仁木, 阿江榄仁酸, 植物化学, 护心活性, 抗菌活性

Phytochemistry and Pharmacological Potential of *Terminalia arjuna* L.

Z. M. Halleys Khan , Hossain Md. Faruquee , Md. Munan Shaik
Department of Biotechnology and Genetic Engineering, Islamic University, Kushtia-7003, Bangladesh
Corresponding author, munanbt2004@gmail.com; mmshaik@btge.iu.ac.bd Authors

Abstract　To cure human diseases, medicinal plants have been a major source of therapeutic agents since ancient time. *Terminalia arjuna* is one kind of widely used medicinal plant throughout Bangladesh and used in various indigenous system of medicine like Ayurveda, Sidda and Unani. This plant has been reported to contain active constituents including arjunolic acid, gallic acid, terminic acid, pyrocatechols, β-Sitosterol, calcium, magnesium, zinc, copper etc., which proved to be effective pharmacological agents as antimicrobial, anticancer, antidiabetic, antiacne, antihelmintic, antiinflammatory, anticholinesterase, antioxidant, antiasthmatic as well as wound healing, cardioprotective and insecticidal activities. It is considered to be an ideal agent for treating cancer, coronary artery disease, hypertension and ischemic cardiomyopathy. The present comprehensive update review is therefore an effort to give detailed information on phytochemical and pharmacological studies of *T. arjuna*.

Keywords　*Terminalia arjuna*; Arjunolic acid; Phytochemistry; Cardio-protective activity; Antimicrobial activity

印斯榄仁木是一个孟加拉本土树种，单叶、树皮厚且光滑，属于使君子科。花小且齐、无柄，杯状，单雄蕊多雌蕊，白色、奶白或淡白绿色，强烈的蜂蜜香味，花期 4 月到 7 月。花序基部有短尖刺，或小的末端圆锥花序；水果为长倒卵形，暗棕色到红棕色，木质纤维，核果，果皮不裂，成熟期 2 月到 5 月(Orwa et al., 2009; Bhat et al., 2003)。从古代开始，由于其治疗患者的功效，印斯榄仁木整体植株都可以利用。印斯榄仁木有助于保持一个健康的心脏，减少压力和焦虑的影响(Emran et al., 2011)。它有抗菌(Perumalsamy et al .,1998)、抗诱变、降血脂、抗氧化、降血脂和抗炎作用(Tripathi et al .,2005)。印斯榄仁木通过增强抗氧化防御作用保护肝脏和肾脏组织对抗由 CCl4 引起的氧化胁迫(Manna et al., 2006)。其化学成分有胃保护作用(Devi et al., 2007)。从这个药用植物中已经提取得到不同类型的生物活性化合物，其在医学中具有巨大的价值，其中阿江榄仁酸很有名。本研究旨在如实阐明印斯榄仁木的植物化学成分和药理特性。

1 植物化学

最初报道称，树皮灰分含量为 34%，完全由纯碳酸钙组成。水提取物包括 23%钙盐和 16%丹宁酸，而酒精萃取物几乎不含色素和单宁(Dymock et al .,1891)。树皮的化学分析证实，糖分、丹宁(12%)、色素、配糖体和碳酸盐中的钙、钠和碱金属中的氯都有存在(Ghoshal, 1909)。印斯榄仁木的化学成分见表 1。

表 1 印斯榄仁木不同部位的主要化学成分
Table 1 Major chemical constituent in different parts of *T. arjuna*

Compounds	Stem/ bark	Root	Activity of compounds	References
Triterpenoids	Arjunin, arjunic acid, arjunolic acid, arjungenin, terminic acid	Arjunic acid, arjunolic acid, oleanolic acid, terminic acid	Antifungal, cardioprotective	Zhou et al., 2011a; Dwivedi, 2007
Glycosides	Arjunetin, Arjunaphthanoloside, Arjunoside I, II and Terminoside-A	Arjunoside I-IV Glucopyranoside	Cardioprotective	Dwivedi, 2007
Sitosterol	Sitosterol	Sitosterol	Antimutagenic, antiinflammatory, antitussive	Zhou et al., 2011d and Dwivedi, 2007
Flavonoids	Arjunolone, Arjunone, Bicalein, Luteolin, Gallic acid, Ethyl gallate Kempferol, Proanthocyanidins, Quercetin, Pelorgonidin,		Antiallergic, antibacterial, cytotoxic, antiasthmatic, antifungal, antioxidant	Zhou et al., 2011b,c,d and Dwivedi, 2007
Tannins	Pyrocatechols, Casuarinin, Casurin, Punicallin, Punicalagin, Castalagin, Terchebulin, Terflavin C,		Astringent, wound healing and antimicrobial	Dwivedi, 2007
Trace elements	Calcium, Aluminium, Magnesium, Silica, Zinc, Copper		To fill up ion requirement	Dwivedi, 2007

表 2 印斯榄仁木分离出的化合物的独特功能和属性
Table 2 Individual functions and properties of some compounds isolated from *T. arjuna*

Compounds	Biological activity	References
Arjunolic acid ($C_{30}H_{48}O_5$, MW: 488.71)	Antifungal, cardioprotective	Zhou et al., 2011a
Arjunic acid ($C_{30}H_{48}O_5$, MW: 488.71)	-	
Arjunglucoside I ($C_{36}H_{58}O_{11}$, MW: 666.86)	-	
Arjungenin ($C_{30}H_{48}O_6$, MW: 504.71)	-	
Castalagin ($C_{41}H_{26}O_{26}$, MW: 934.65)	Antihypertensive, cytotoxic	
Ethyl gallate ($C_9H_{10}O_5$, MW: 198.18)	Antibacterial (Bacillus dysenteriae), antifibrotic, platelet aggregation inhibitor, collagenase inhibitor, analgesic	Zhou et al., 2011b
Gallic acid ($C_7H_6O_5$, MW: 170.12)	Antiallergic, antibacterial, antineoplastic, cytotoxic, antifungal, anti-inflammatory, antimutagenic, antiviral, astringent, antiasthmatic; choleretic, antioxidant cell growth inhibitor, control phosphoramidon	
Luteolin ($C_{15}H_{10}O_6$, MW: 286.24)	Antiallergic, antibacterial, antineoplastic, cytotoxic, antifungal, anti inflammatory, antispasmodic, antitussive, immunoenhancer, increases coronary flow, protein kinase C inhibitor, succinic oxidase inhibitor, antihypercholesterolemic	Zhou et al., 2011c
Kaempferol ($C_{15}H_{10}O_6$, MW: 286.24)	Anti-HIV-1, antibacterial, antitussive to cure trachitis, antioxidant, iodinate thyronine deiodinase inhibitor, aldose reductase inhibitor, anti-inflammatory	
B-Sitosterol ($C_{29}H_{50}O$, MW: 414.72)	Antineoplastic, antimutagenic anti-inflammatory, antitussive, antihypercholesterolemic	Zhou et al., 2011d
Chebulinic acid ($C_{41}H_{34}O_{28}$, MW: 974.75)	-	Singh, 2002
Proanthocyanidin B2 ($C_{30}H_{26}O_{12}$, MW: 578.53)	Anticomplement activity, antihypertensive, protein kinase C inhibitor, reverse transcriptase inhibitor, antioxidant	Zhou et al., 2011d
Terchebulin ($C_{48}H_{28}O_{30}$, MW: 1084.74)	-	Zhou et al., 2011e
Terminoic acid ($C_{30}H_{48}O_5$, MW: 488.71)	-	
Terflavin A ($C_{48}H_{30}O_{30}$, MW: 1086.76)	-	

表 3 印斯槐仁木不同溶剂提取物的抗菌活性
Table 3 Antimicrobial activity of different solvent extracts from *T. arjuna*

Solvents	Organisms	Extracts concentration	Highest activity showed extract	Maximum zone of inhibition (mm)	Highest sensitivity showed organisms	References
Methanol, Ethanol, Acetone, Hot aqueous, Cold aqueous	*Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Proteus mirabilis*, *Escherchia coli*, *Acitenobacter* sp. *Candida albicans*	50 mg/mL	Acetone	28	*Staphylococcus aureus*	Aneja et al., 2012
Aqueous, Methanol	*Staphylococcus aureus*, *Bacillus cereus*, *Escherichia coli*, *Vibrio cholerae*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*	Aqueous 2 gm/20 mL, Methanol 30 mg/mL	Methanol	0.625±0.016	*Escherichia coli*	Dey et al., 2010
Methanol, Ethyl alcetate, Acetone, Gemmo-modified, Water	*Staphylococcus aureus*, *Bacillus subtilus*, *Escherichia coli*, *Pasteurella multocida*	250µg/disc, 500 µg/disc, 750 µg/disc, 1000 µg/disc	1000 µg/disc (Gemmo-modified)	38±1.0	*Bacillus subtilus*	Jahan et al., 2011
Crude and Methanol	*Streptococcus pneumoniae*, *Staphylococcus aureus*, *Salmonella typhi*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Yersinia enterocolitica*, *Candida albicans*	1 g/5 mL	Methanol	30	*Staphylococcus aureus*	Elizabeth, 2005
Ethanol	*Staphylococcus aureus*, *Streptococcus faecalis*, *Coliform spp.*, *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*	25 µg/mL, 50 µg/mL, 100 µg/mL, 200 µg/mL	Ethanol (200 µg/mL)	20	*Coliform spp.*	Emran et al., 2011
Ethanol	*Bacillus subtilis*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella pneumonia*, *Salmonella typhi*		0.5 mg/disc, 1 mg/disc Ethanol (0.5 mg/disc)	16	*Staphylococcus epidermidis*	Kannan et al., 2009
Aqueous, Methanol	*Staphylococcus aureus*, *Escherichia coli*,	10%, 15% Aqueous; 10%, 15% Methanol	15% Methanol	13	*Staphylococcus aureus*	Seniya et al., 2011

2 生物活性化合物

由于印斯槐仁木含有不同的生物活性化合物在人体和动物中表现生物活性，其具有药用价值和经济价值(Zaidi, 1998)。截止目前，报道出的一些有活性的生物活性化合物见表 2。

3 药理价值

之前有许多研究报道印斯榄仁木大量的药理活性。它可以用来治疗糖尿病、心脏疾病，治疗伤口。它具有抗病毒、抗菌、抗癌和其他潜在的治病属性。

(i)抗菌活性：Perumalsamy 等(1998)报道，印斯榄仁木的树皮水提取物对变形杆菌、克雷伯氏菌、大肠杆菌、假单胞杆菌具有抗菌活性。印斯榄仁木树皮的抗菌反应表现出选择性地对表皮葡萄球菌有最大抗菌活性(Singh et al., 2008)。印斯榄仁木不同溶剂提取物的抗菌活性总结见表 3。

(ii)抗癌活动：不同类型的癌症治疗报道了印斯榄仁木提取编译在表 4。据印斯榄仁木草药提取物提高的百分比增加寿命的实验动物诱导与国防后勤局道尔顿淋巴瘤腹水肿瘤细胞和在某些情况下与致癌物诱导(Muthuchelian et al .,2010)。印斯榄仁木提取物诱导 HepG2 细胞 DNA 损伤表明，印斯榄仁木提取诱发 HepG2 细胞中活性氧的生产，从而导致细胞凋亡(Sarveswaran et al., 2006)。

表 4 印斯榄仁木提取物治疗各种癌症
Table 4 Different types of cancers and their treatment by *T. arjuna* extracts

Types of cancers	Used extracts	Active compounds	Treated organisms/cells	References
Mutagenic cancer	Dried bark	Tannin	*Salmonella typhimurium*	Kaur et al., 2000
Human breast, colon,intestine, lung and leukaemia.	Leaf	Taxol	*Pestalotiopsis terminaliae*	Gangadevi et al., 2009
Ehrlich ascites carcinoma (EAC)	Methanolic extract of Leaves	-	Mice	Biswas et al., 2012
Human breast	Bark	Casuarinin	Human breast adenocarcinoma MCF-7 cell	Kuo et al., 2005
Age related cancer	Aqueous bark extract	Catalase, superoxide dismutase and glutathione S transferase	*Lymphoma bearing mice*	Verma et al., 2005
BT- human breast	Ethanolic extracts of leaves	Ellagenatin (arjunin)	BT-human breast carcinoma cells	Kandil et al., 1998

(iii)对耳朵感染：印斯榄仁木植物提取物开发潜力巨大,草药耳坠来控制细菌的耳部感染。Aneja 等(2012)报道，树叶和树皮提取物作为一种有效的和有效的医学测试细菌负责耳部感染比标准的耳坠。

(iv)抗真菌活性：对五种榄仁树属物种的有机提取物(印斯榄仁木、诃黎勒树、红果榄仁果树、枇杷树和翅榄仁木)进行植物病原真菌(黄曲霉、细极链格孢、黑曲霉、黑斑病菌和四胞长蠕孢)测试。所有五种植物的叶子提取物对这些植物病原体都表现抑制作用(Shinde et al., 2011)。这次抗菌测试中，树皮提取物比杀菌剂(对照)更有效。阿江榄仁酸混合物的最低抑制浓度(MIC)值范围为 50~200 μg/mL 时，对白色念珠菌、克柔假丝酵母菌、近平滑念珠菌表现出温和的抗真菌活性(Puvanakrishnan et al., 2010)。

(v)抗糖尿病活性：印斯榄仁木提取物对糖尿病有潜在影响。使用印斯榄仁木提取物饲喂实验性糖尿病大鼠模型中，葡萄糖-6-磷酸酶和果糖-1,6-二磷酸酶在肝脏和肾脏中活性显著降低。这对增加胰岛素分泌有影响，从而抑制糖异生关键酶(葡糖激酶和磷酸果糖激酶) (Ragavan et al., 2006)。印斯榄仁木树皮提取物的抗糖尿病活性是通过加强葡萄糖的次生代谢来实现的，加强肾脏的糖酵解，纠正受损肝脏，形成胰岛素等抑制糖异生。这种效应可能是因为树皮中含有单宁、皂苷、黄酮类化合物及其他成分，可独立或协同增强糖酵解和糖异生中酶的活性(Ragavan et al., 2006)。Manna 等(2009a; 2009b)用瑞士白化大鼠的胰腺组织，研究了阿江榄仁酸对链脲霉素(STZ)诱导的糖尿病的预防性作用。STZ 的使用(用药剂量为每公斤体重 65 mg，尾静脉注射)导致实验动物的胰腺中活性氧(ROS)和活性氮(RNS)增加。这些活性中间体的形成降低了细胞内的抗氧化防御，提高脂质过氧化、蛋白质羰基化、血清葡萄糖和 TNF-α 水平(Puvanakrishnan et al., 2010)。

(vi)祛痘作用：含有类黄酮(FF-I, FF-II, FF-III)和丹宁成分(TF-I, TF-II, TF-III)的印斯榄仁木提取物外用配方(面霜)已经被开发出来，用其对疮疱丙酸杆菌和表皮葡萄球菌进行抗菌活性检测。相较于其他配方，FF-III 配方(奶油含有黄酮类分数 2%)对疮疱丙酸杆菌(抑制范围大于 17 mm)和表皮葡萄球菌(抑制范围大于 20 mm)表现高抗菌活性，可以比得上标准的市售外用草药制剂(Vijayalakshmi et al., 2011)。植物祛痘霜是无毒、安全、有效的，使用印斯榄仁木草药提取物可以提高病人的可塑性，将会被广泛接受(Vijayalakshmi et al., 2011)。

(vii)驱虫活性：在体外(卵、幼虫和捻转血矛线虫成虫)和体内(对羊混合胃肠毛圆线虫用药研究)试验中，印斯榄仁木树皮酒精粗提物均表现抗虫活性(Bachaya et al., 2009)。印斯榄仁木树皮的驱虫活性可能主要归因于其

单宁含量，其与游离蛋白质结合，存在于幼虫营养管，减少养分有效性，导致幼虫饥饿或通过直接抑制氧化磷酸化减少胃肠道代谢，造成幼虫死亡(Bachaya et al., 2009)。

(viii)伤口愈合活性：据报道，印斯榄仁木树皮的水醇提取物被用于大鼠皮肤创伤治疗外用。如同其他简单药膏，使用各种剂量对麻醉大鼠背部伤口进行外敷。结果证明，第三种剂量下，只有简单药膏的 1%，完整的上皮形成需 20 天；而第三种剂量下，完整上皮形成需 9 天，实质上包括单宁的作用(Puvanakrishnan et al., 2010)。Mengi 等(2003)报道了印斯榄仁木在切口创伤上皮愈合和增加切口创伤抗拉强度上的能力。

(ix)心血管活动：基于各种古代医学中记录的经验解释，心脏疾病有多种印斯榄仁木治疗方法。

(a)强心活性：在阿育吠陀医学中阿江榄仁酸用于心脏病治疗已经有几个世纪了，首次提取是从印斯榄仁木得到的。其树皮提取物的主要成分三萜皂苷是一种阿江榄仁酸(Puvanakrishnan et al., 2010)。在离体兔子和青蛙的心脏中进行的生理性研究表明，印斯榄仁木树皮具有强心和刺激作用(Ghoshal, 1909)。结果发现，用印斯榄仁木树皮得到的配糖体进行静脉注射导致了血压的上升(Ghosh, 1926)。表明，其树皮粉有强心特性和利尿特性。之后的青蛙心脏离体试验研究发现，印斯榄仁木树皮水提物具有心肌变时性和心肌收缩活性。在离体大鼠心房中证实了印斯榄仁木树皮水提物具有正性肌力作用(Radhakrishnan et al., 1993)。后续工作中使用心得安和可卡因抑制离体大鼠心房的变力作用，而印斯榄仁木树皮水提物在其中发挥作用(Karamsetty et al., 1995)。印斯榄仁木根部分离出一种新化合物，16,17-Dihydroneridienone,3-O- β - Dglucopyranosyl-(1-6)-O- β -D-galactopyranoside 被用作了强心剂(R.N. Yadav et al., 2001)。

(b)冠状流：Bhatia 等(1998)报道，使用印斯榄仁木树皮水提物进行兔子离体心脏灌流(Langendorff)会增加冠状流。1 024 μg/mL 的剂量引起的冠状动脉流量增加最大。

(c)低血压的影响：Singh 等(1982)报道，树皮的酒精溶液抽提物在脊柱内注射和侧脑室注射，会引起持久的剂量依赖的心动过缓和低血压。而且，其酒精萃取物引起阿托品预处理的狗低血压。在狗的另一项研究表明，静脉注射印斯榄仁木的抽提物水溶液导致血压的剂量依赖下降(Srivastava et al., 1992)。

(d)对主动脉前列腺素的影响：兔子试验中，饲喂印斯榄仁木的比使用安慰剂的兔子，在主动脉前列腺素 E2 的活动上表现加强。PGE2 引起冠状动脉舒张，提高 PGE2 类的活性是有意义的。这可能解释了印斯榄仁木灌注后引起冠状动脉流量增加的药理基础(Bhatia et al., 1998)。鉴于此，印斯榄仁木的有益作用将为在冠状动脉疾病(CAD)的病人带来福音。

(x)抗炎：Sharma 等(2010)证明，包含曼佗罗(叶)、印斯榄仁木(树皮)和南非醉茄(根)的酒精粗提物的草药复方制剂具有抗炎作用，抑制了环氧合酶(COX)的作用，导致前列腺素合成引发炎症反应的第三阶段被抑制。此研究结果标明，具有显著抗炎、镇痛功效的草药复方制剂是可以制成的(Puvanakrishnan et al., 2010)。

(xi)杀虫特性：对尘白灯蛾四龄幼虫，印斯榄仁木茎分离出的阿江榄仁酸表现显著的抑制作用。减少喂养的有效浓度是 617.8 ppm，幼虫增长的有效浓度分别是 666.9 ppm (Puvanakrishnan et al., 2010)。

(xii)抗氧化活性：抗氧化测试中，印斯榄仁木树皮的甲醇提取物方面表现出显著的抗氧化作用，IC50 值为 7.05 μg/mL。印斯榄仁木的甲醇提取物表现抗氧化活性，有药物利用潜力(Rahman et al., 2011)。

(xiii)抗哮喘活性：阿江榄仁酸和印斯榄仁木的酒精萃取物有明显的肥大细胞稳定作用，具体来说，阿江榄仁酸的作用比 TA 酒精提取物表现出相对更好的稳定性(Prasad et al., 2004)。抗哮喘和抗过敏作用可能是由于肥大细胞稳定的潜力以及诱导组胺和乙酰胆碱释放的抗原的抑制作用(Prasad et al., 2004; Puvanakrishnan et al., 2010)。

(xiv)胃保护效应：由于其自由基清除活性和细胞保护属性，印斯榄仁木可以充当胃保护药剂(Devi et al., 2007)。

(xv)减少砷诱导毒性：阿江榄仁酸对砷诱导细胞氧化应激的预防作用(Sil et al., 2007)。

4 传统应用

阿育吠陀医疗体系中，印斯榄仁木被广泛应用，并被熟知。因其在不同类型的心脏疾病，包括高血压、心绞痛和块动脉上的疗效，印斯榄仁木得以被医生利用。在治疗疼痛相关的疾病，比如，心力衰竭、精溢、瘀斑、淋病等性传播疾病上，它也非常有用。印斯榄仁木被认为是一个有用的止血药、降温药、壮阳药、强心剂，用于溃疡、白带异常、糖尿病、咳嗽、肿瘤、过度出汗、哮喘、炎症和皮肤病等治疗中(Parakh, 2010)。

5 印斯榄仁木的体外繁殖

由于缺乏优化的管理策略、伐木、林地转农田，原生森林的自然再生普遍跟不上森林砍伐速度，不同类型的物种受到威胁，处于濒危(IUCN 2011)。Pijut 等(2012)报道了不同地区印斯榄仁木的体外繁殖。4.44μM BA+0.53μM NAA 半强度 MS 培养基上，使用成熟植株的外植体节点繁殖印斯榄仁木。4 月或 5 月所采集材料的最佳扩散率被发现受季节性变化的影响。4.92μM IBA 培养基可以生根，植物表现出适应性(Pandey et al .,2006)。

6 结论

目前的研究显示，印斯榄仁木是一种非常重要的植物，其含有大量的植物化学和药理性质，以及药用方面很重要的化学成分。人们发现其在抗菌、抗病毒、抗诱变、抗炎和伤口愈合中是非常有用的。最令人兴奋的是，它可以治疗糖尿病、癌症和心脏疾病。本综述的观点是：印斯榄仁木存在各种潜在的药用特征。因此，本研究为愿意对印斯榄仁木的草药和草药复方制剂开发进行深入研究和系统研究的研究人员提供了初步的真实的原始资料。

作者贡献

Khan Z.M.H.和 Faruquee H.M.进行试验设计；Shaik M.M.进行项目设计；Shaik M.M. and Faruquee H.M.进行数据分析；Shaik M.M.、Faruquee H.M.和 Khan Z.M.H.完成论文写作。

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