

Invited mini review

Butein: From ancient traditional remedy to modern nutraceutical



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ABSTRACT

Butein (2',3,4,4'-tetrahydroxychalcone), a simple chalcone derivative, occurs in many unrelated genera including *Butea Dahlia*, *Coreopsis* and *Searsia*. It is a reputed food additive and a common ingredient of botanicals used in herbal medicine formulations, particularly in Asian countries. Although a simple polyphenol, this molecule exhibits a range of pharmacological properties, most notably acting as a potent protein tyrosine kinase inhibitor and as an antineoplastic agent. Researchers have convincingly demonstrated that butein inhibits the epidermal growth factor receptor in HepG2 cells and the tyrosine-specific protein kinase activities of the epidermal growth factor receptor. In addition, it also exhibits promising anti-inflammatory, antidiabetic, antinephritic, antithrombin, anti-angiogenic and hepato-protective activities in various animal models. Although this molecule is endowed with an impressive list of biological properties, which have acted as scientific support for its commercialization, there are no review articles that coherently discuss various aspects of this chalconoid. This review aims to explore the pharmacological relevance of butein, together with its structure–activity relationships and mechanisms of action. In addition, the occurrence, chemical synthesis and biosynthesis of butein are discussed.

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Abbreviations: ADP, adenosine diphosphate; BDE, bond dissociation energy; BHT, butylated hydroxytoluene; COX, cyclooxygenase; DPPH, diphenyl-2-picrylhydrazyl; EGFR, epidermal growth factor receptor; ERK, extracellular signal-regulated kinase; HPLC, high performance liquid chromatography; HSC, hepatic stellate cells; ICAM, intercellular adhesion molecule; IL, interleukin; iNOS, inducible nitric oxide synthase; JNK, c-Jun N-terminal kinase; LPS, lipopolysaccharide; MMP, matrix metalloproteinase; NF- κ B, nuclear factor-kappa B; NO, nitric oxide; Nrf2, Nuclear factor-like-2; PARP, poly(ADP-ribose) polymerase; PDGF, platelet-derived growth factor; PMA, phorbol 12-myristate 13-acetate; ROS, reactive oxygen species; STAT, transducer and activator of transcription; TGF, transforming growth factor; TNF, tumour necrosis factor; TRAIL, tumour necrosis factor-related apoptosis-inducing ligand; VEGF, vascular endothelial growth factor.

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1. Introduction

Butein, chemically described as 2',3,4,4'-tetrahydroxychalcone (Fig. 1), is a chalcone derivative produced by species from several diverse botanical families, including the Anacardiaceae, Asteraceae and Fabaceae. The genera *Dahlia*, *Butea*, *Searsia* and *Coreopsis* are most often used as sources for isolation purposes (Table 1). The compound was first isolated and identified in 1904 from the flowers of *Butea frondosa*, in the form of a yellow

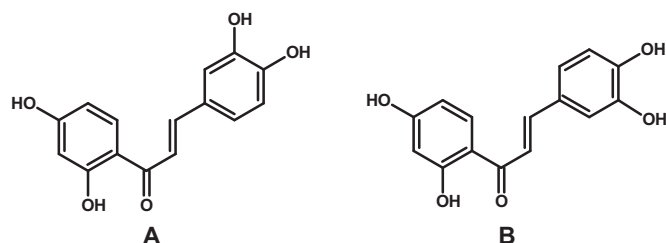


Fig. 1. Chemical structure of butein. (A) Stable isomer; (B) less stable isomer.

colouring pigment (Perkin and Hummel, 1904). However, Perkin and Everest (1918) proposed that butein is not produced by *B. frondosa*, but rather, that it is a biotransformation product of butin that is formed during the drying or extraction of the flowers. Schmid and Seebald (1932) purified butein from flowers of *Dahlia variabilis*. Although the compound could not be identified, they reported that it was chemically distinct from apigenin, which at that stage was thought to be the only coloured substance present in the flowers of *D. variabilis*. This yellow colourant was later identified by Price (1939), who incorrectly stated that *D. variabilis* was the first identified natural source of butein.

Butein is an important dietary polyphenol. It has been recognised for its ability to inhibit the enzyme protein tyrosine kinase (Yang et al., 1998), thereby preventing phosphorylation and affording protection against some cancers and inflammatory diseases (Samoszuk et al., 2005). It has promising chemopreventive and chemotherapeutic potential (Orlikova et al., 2011). Butein is a popular ingredient of various herbal drug formulations and is widely used as a nutraceutical, particularly in Asian countries (Dan and Gamble, 1993). The compound displays inhibitory effects

Table 1
Occurrence of butein in various plant species from different families.

Family	Plant	Part	Reference	
Adoxaceae	<i>Viburnum propinquum</i> Hemsl.	Leaves	Wang et al. (2009a)	
Anacardiaceae	<i>Cotinus coggygia</i> Scop.	Heartwood	Antal et al. (2010), Valianou et al. (2009)	
	<i>Searsia verniciflua</i> Stokes Syn.	Stem bark	Lee et al. (2002), Jeon et al. (2006)	
	<i>Toxicodendron vernicifluum</i> (Stokes) FA Barkley	Stem bark	Lee et al. (2002), Jeon et al. (2006)	
	<i>Semecarpus anacardium</i> L.	Stem bark	Pandey et al. (2007)	
Asparagaceae	<i>Sansevieria liberica</i> Ger. and Labr.	Rhizomes	Ikwuchi et al. (2011)	
Asteraceae	<i>Bidens bipinnata</i> L.	Flowers	Kwon et al. (2009)	
	<i>Bidens pilosa</i> L.	Whole plant	Tian et al. (2011)	
	<i>Bidens tripartita</i> L.	Whole plant	Serbin et al. (1974)	
	<i>Coreopsis douglasii</i> (DC.) HM Hall	Flowers	Geissman (1941a)	
	<i>Coreopsis gigantea</i> (Kellogg) HM Hall	Flowers	Geissman (1941b)	
	<i>Coreopsis maritima</i> (Nutt.) Hook. f.	Flowers	Geissman et al. (1956)	
	<i>Coreopsis petrophiloides</i> BL Rob. & Greenm.	Flowers	Crawford (1978)	
	<i>Coreopsis lanceolata</i> L.	Flowers	Shimokoriyama and Hattori (1953)	
	<i>Cosmos sulphureus</i> Cav.	Flowers	Geissman (1942)	
	<i>Dahlia variabilis</i> Desf.	Flowers	Schmid and Seebald (1932)	
	<i>Dahlia coccinea</i> Cav.	Petals	Harborne et al. (1990)	
	<i>Vernonia anthelmintica</i> Willd.	Seeds	Tian et al. (2004)	
	Fabaceae	<i>Acacia pycnatha</i> Benth.	Heartwood	Roux and Paulus (1961)
		<i>Adenanthera pavonina</i> L.	Wood	Gennaro et al. (1972)
<i>Bauhinia purpurea</i> L.		Seeds	Bhartiya et al. (1979)	
<i>Butea frondosa</i> Roxb.		Flowers	Perkin and Hummel (1904) Murti and Seshadri (1940)	
<i>Butea monosperma</i> (Lam.) Taub.		Flowers	Lau et al. (2010)	
<i>Caragana intermedia</i> Kuang & HC Fu Syn.		Whole plant	Shi et al. (2003)	
<i>Caragana korshinskii</i> Kom.				
<i>Cyclopia subternata</i> Vogel Syn.		Seeds	De Nysschen et al. (1998)	
<i>Cyclopia falcata</i> (Harv.) Kies				
<i>Dalbergia odorifera</i> TC Chen		Heartwood	Yu et al. (1995), Liu et al. (2005)	
<i>Dipteryx lacunifera</i> Ducke	Fruits	Junior et al. (2008)		
<i>Milletia nitida</i> var. <i>hirtutissima</i> Z. Wei	Stems	Liao et al. (2013)		
<i>Milletia speciosa</i> Champ.	Roots	Wang et al. (2008)		
<i>Sophora alopecuroides</i> L.	Whole plant	Wang and Ma (2009)		
<i>Vicia faba</i> L.	Fruits	Tomas-Barberan et al. (1991)		
Pinaceae	<i>Abies pindrow</i> Royle ex D. Don	Stems	Tiwari and Minocha (1980)	
Rubiaceae	<i>Hydnophytum formicarum</i> Jack.	Tubers	Prachayasittikul et al. (2008)	
Schisandraceae	<i>Schisandra propinqua</i> (Wall.) Baill	Whole plant	Wu et al. (2010)	
Solanaceae	<i>Solanum lycopersicum</i> Lam.	Fruits	Schijen et al. (2006)	

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