Phytochemicals and Their Biological Activities of Plants in *Tagetes* L.

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Abstract: *Tagetes* L., the genus in the family Asteraceae, consists of about 30 species spread in South and Middle America as well as Mexico. More than one hundred secondary metabolites have been obtained in phytochemical investigation on the species, some of which have potent biological activities. The advances in phytochemical studies and biological activities of the plants in *Tagetes* L. from 1925 to 2011 are summarized in this paper.

Key words: Asteraceae; biological activities; secondary metabolite; *Tagetes* L.
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Introduction

The plants in *Tagetes* L., popularly known as marigold, is originally used as an ornamental plant (Wang, Xu, and Zhao, 2002). There are about 30 species in *Tagetes* L. in South and Middle America as well as Mexico. Both *T. erecta* L. and *T. patula* L. are mainly distributed in China. *T. erecta* has been widely cultured in China and *T. patula* is mainly cultured in Guizhou, Yunnan, Guangdong, Hainan, and Guangxi Provinces of China. The species of *Tagetes* L. have not been admitted in *Chinese Pharmacopoeia 2010*, however, their chemical compounds and bioactivities have been intensively studied in recent years. The phytochemical studies of the plants in *Tagetes* L. could be traced back to 1920s. Till now, about 126 secondary metabolites with various carbon skeletons, phenolic derivatives, phenylpropanoids, thiophene derivatives, benzofunan derivatives, triterpenoids, steroids, alkaloids, flavonoids, carotenoids, and others have been obtained from the species of *Tagetes* L. Some of them showed potent activities as leading compounds of the new drugs.

Some species in *Tagetes* L. have been widely used as folk medicine for calming the liver, dominating heat, expelling wind, and reducing phlegm (Lin, 2009), and also have been used as natural insecticides and fungicides (Vasudevan, Kashyap, and Sharma, 1997). For example, the extract from the roots of *T. erecta* was lethal or inhibitory to the hatching of *Meloidogyne javanica* (Treub) Chitw. and *M. arenaria* (Neal) Chitwood (Vasudevan, Kashyap, and Sharma, 1997). The extracts from some species in *Tagetes* L. also exhibited antifungicidal activity (Vasudevan, Kashyap, and Sharma, 1997). Various oils in plants of *Tagetes* L. were found to inhibit Gram-positive bacteria and fungi (Vasudevan, Kashyap, and Sharma, 1997). In addition, flower pigments in the plants of *Tagetes* L., as natural colorant, have been widely used in food and drink (Vasudevan, Kashyap, and Sharma, 1997). Other applications, such as the anti-oxidative and anti-mutagenic activities, have also emerged, which gradually captured the interest of scientists.

The lack of updated reviews on this topic urged us to speculate the topic from phytochemical and biological views.

Chemical constituents

Phenolic derivatives

Four phenolic derivatives (**1** — **4**) have been isolated from the species of *Tagetes* L. Among them, the positions C-1 and C-4 are substituted by -COOH and -OH, respectively, while no substitution occurs at the position C-2 or C-6. The positions C-3 and C-5 are often substituted by -OMe or -OH.

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Phenylpropanoids

Six phenylpropanoids (**5**—**10**) isolated from plants in *Tagetes* L. have been reported. Compounds **7** and **8** are a pair of isomers with differences at the configuration of the positions C-1, C-3, C-4, and C-5. Compounds **9** and **10** are two classical coumarin derivatives.

Thiophene derivatives

Sixteen thiophene derivatives (**11** — **26**) in the species of *Tagetes* L. have been identified. α-Terthienyl (**11**) was discovered from the flowers of the lemon variety of *T. erecta* by Zechmeister and Sease in 1947 (Vasudevan, Kashyap, and Sharma, 1997). Compound **13** was identified in 1959. Then, in 1962, compounds **17**, **21**, **22**, and **25** were isolated from the ether extracts of *T. erecta* and *T. patula* (Wang, Xu, and Zhao, 2002). Compounds **14** and **15** were reported in 1964 by Atkinson *et al* (Wang, Xu, and Zhao, 2002). The others were reported subsequently during the years 1966—2011. α-Terthienyl is representative in this class of compounds. It is found to distribute in five species, *T. erecta* Linn., *T. patula* Linn., *T. tenuifolia* Cav., *T. microglossa* Benth., and *T. jalisciencis*.

Among these compounds, **13**—**26** are bithiophene derivatives, of which substituted groups are introduced to the positions C-5 and C-5′. Alkyne rarely appeared as a substituted group. However, from this genus, nine bithiophenes (**14** — **17**, **21** — **24**, and **26**) were substituted with alkynes. The biosynthesis study of 5-(3,4-diacetoxy-1-butynyl)-2,2′-bithiophene (**16**) showed that the compound **16** was converted to 5-(3,4-dihydroxy-1-butynyl)-2,2′-bithiophene by a highly specific 5-(3,4-diacetoxy-1-butynyl)-2,2′-bithiophene: 4-acetate esterase, and 5-(3-hydroxy-4-acetoxy-1-butynyl)-2,2′-bithiophene was the intermediate product in the process (Pensl and Sűtfeld, 1985). Compound **22** was yielded by biosynthesis in root cultures which was grown with [U-$^{13}C_6$] glucose or [1-^{13}C] glucose of *T. patula*, and the data suggested that acetyl-CoA or a closely related compound (e.g. malonyl-CoA) might be as building blocks and their orientations in the bithiophene (Margl *et al*, 2001).

Benzofunan derivatives

Six benzofunan derivatives (**27** — **32**) were identified in the species of *Tagetes* L. Their names, structures, and resources were listed in Table 1. The structures of the compounds were determined by spectral analysis and compared with published data. The molecular structure of isoeuparin (**27**) was characterized by single crystal X-ray diffraction. What is interesting is that the identified benzofunan compounds only exist in *T. patula*. It may provide evidence to the plant taxonomy in the species of *Tagetes* L.

Terpenoids and steroids

Terpenoids (**33**—**44**) were found and isolated from *T. erecta.* Auto-oxidation often occurred among compounds **37** — **42** (Faizi and Naz, 2004). Auto-oxidation converted compound **37** into compounds **38** and **40**, and transformed compound **38** into compound **42** (Faizi and Naz, 2004). Compound **44**, the only sesquiterpenoid, was also isolated from *T. erecta.* However, five steroids, compounds **45**—**49**, were also isolated from *T. erecta* and *T. patula*.

Alkaloids

To date, two alkaloids (**50**—**51**) are found from this genus. Jafrine (**50**) is an inherently unstable and structurally novel tetrahydro-β-carboline alkaloid (Faizi and Naz, 2002). Auto-oxidation made jafrine transform into 2-acetyl tryptamine derivatives (Faizi and Naz, 2002). Liu, Su, and Wang (2007) reported that alkaloids with different polarity indeed existed in the roots of *T. erecta*. However, the chemical components have not been investigated, and further investigation is called for.

Flavonoids

Flavonoids are the main components within the genus *Tagetes* L., and may have the meaning of chemosystematic interpretations in some extent. A total of forty-nine flavonoids (**52**—**100**) have been identified from the genus *Tagetes* L. Flavonoids exist within this genus in the free or glycoside form. This class within the genus could be divided into two subgroups, flavone derivatives and flavonol derivatives.

Flavone derivatives Only three flavone derivatives have been isolated from the genus. They are luteolin (**52**) from *T. multiflora* Kunth and *T. rupestris* Cabrera, luteolin 7-*O*-glucoside (**53**) from *T. multiflora*, and chrysocriol-7-*O*-(6-*O*-α-*L*-arabinofuranosyl)-β-*D*-glucopyranoside (**54**) from *T. patula.*

Flavonol derivatives Except for compounds **52**—**54**, the flavonoids isolated from the genus belong to the subgroup of flavonol derivatives. All of them bore oxygen functions at the positions C-5, 7, and 4′.