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Review article

Recent synthetic and medicinal perspectives of tryptanthrin

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ABSTRACT

Tryptanthrin is a natural alkaloidal compound having basic indoloquinazoline moiety. It is obtained from various natural plant sources as well as different cell cultures including yeast *etc*. Trptanthrin is considered as biogenetic precursor for phaitanthrin A–C, pyrroloindoloquinazoline, (±)-cruciferane. Different synthetic approaches for the synthesis of tryptanthrin have been very well reported. It has broad spectrum of biological activities including anticancer activity, anti-inflammatory, antiprotozoal, antiallergic, antioxidant, and antimicrobial. In this review, our focus will be, on the various approaches for the synthesis of tryptanthrins and its derivatives along with the biological activities.

1. Introduction

Tryptanthrin is a weak basic, golden yellow, alkaloidal compound. It is an indoloquinazoline alkaloidal antibiotic, chemically written in IUPAC form as (6,12-dihydro-6,12-dioxoindolo-(2,1-*b*)-quinazoline). It consists of a quinazoline ring fused to an indole moiety with carbonyl groups in the 6- and 12-positions as shown in Fig. 1. A large number of tryptanthrin derivatives, natural as well as chemically synthesized, have been observed and bears a different functional group at the sixth position of a common indolo[2,1-*b*]quinazoline core.[1–4] It was first isolated from culture of yeast *Candida lipolytica*[5] and later on isolated from Chinese medicinal plant *Strobilanthes cusia* Kuntze (Acanthaceae).[6,7] It is also obtained from number of other plant species such as *Isatis*, *Clanthe*, *Wrightia*, *Couroupota*.

It has generated great interest as a potential therapeutic agent because of its structural simplicity, convenient to synthesis and broad spectrum of biological activities. Some of these biological properties of tryptanthrin include antifungal activity against various *Trichophyton*, *Microsporum*, and *Epidermophyron* species, anti-growth of *Leishmania donovani*, *Trypanosoma brucei* and *Plasmodium falciparum*, and anti-inflammation *via* inhibiting cyclooxygenase-2 activity or down-regulating the expression of nitric oxide synthase.[8] The *in vitro* antitumor activity of tryptanthrin has been observed in a number of cancer cell lines, including leukemia U937, breast MCF-7, glioma U251, colon SW620, and lung H522[9] whereas *in vivo* antitumor activity of tryptanthrin has also been reported. The most attractive and important biological activity of tryptanthrin is its anti-tuberculotic property. It has been found that tryptanthrin is much more potent against *Mycobacterium tuberculosis*. Furthermore, reports had revealed that tryptanthrin is a potential agent against MDR-tuberculosis.[10] It also possesses other activities such as being antiprotozoal,[11] antioxidant,[5] antimicrobial.[6,12,13] Its effective use against allergy,[14] intestinal disorders,[15] inflammatory bowel disorders,[16] antiparasitic activity[17] has been very well demonstrated.

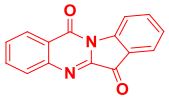

Fig. 1. Structure of tryptanthrin.

2. Synthesis of tryptanthrin

Different synthetic approaches have been utilized for the synthesis of tryptanthrin using different starting materials and reactions conditions as shown in Fig. 2. It is clearly seen that by using one or more starting material and by changing reaction conditions, the formation of tryptanthrin is possible. This is just an overview for the synthesis of tryptanthrin; complete explanation of the synthetic approaches has been described below (Figs. 3–11).

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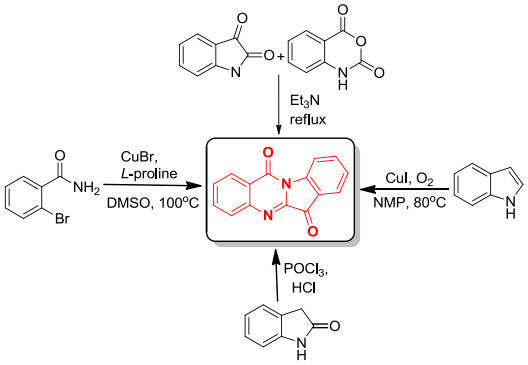


Fig. 2. Different approaches for synthesis of tryptanthrin.

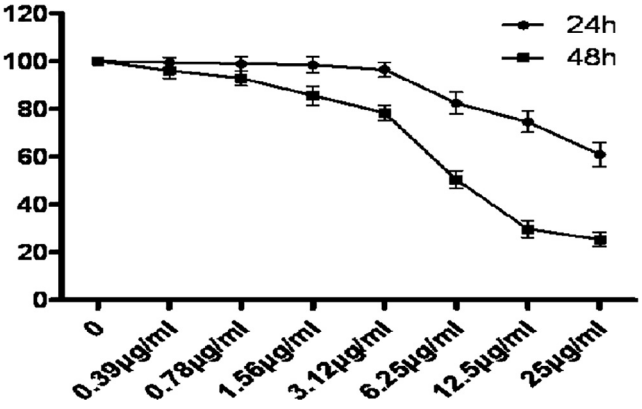
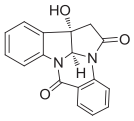


Fig. 6. Effect of tryptanthrin on survival rate of K 562 cell lines.



(+)-55

Fig. 3. Structure of pyrroloindoloquinazoline alkaloid.

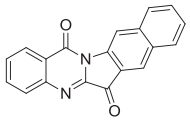


Fig. 7. Benzo[*b*]tryptanthrin.

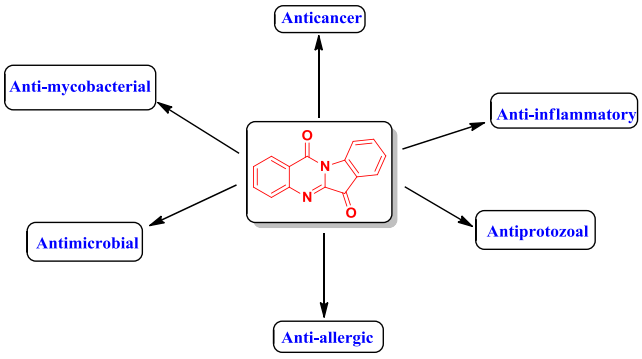


Fig. 4. Schematic representation of biological activities of tryptanthrin.

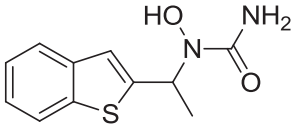
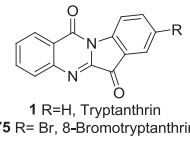


Fig. 8. Structure of Zileuton.



1 R=H, Tryptanthrin
75 R= Br, 8-Bromotryptanthrin

Fig. 9. Structure of antiprotozoal tryptanthrin derivatives.

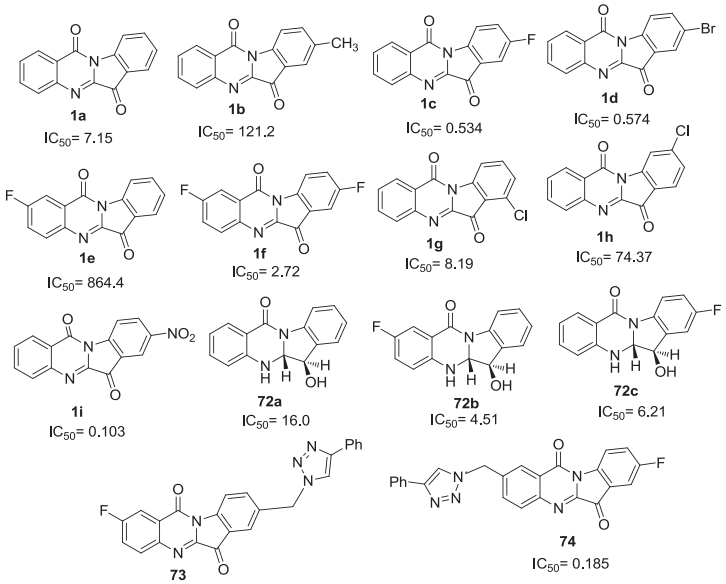


Fig. 5. Compounds with potent inhibitory activity showing IC_{50} value in μM.