

PHYTOCHEMICAL REVIEW PROFILE OF SESQUITERPENE LACTONE PARTHENIN

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ABSTRACT

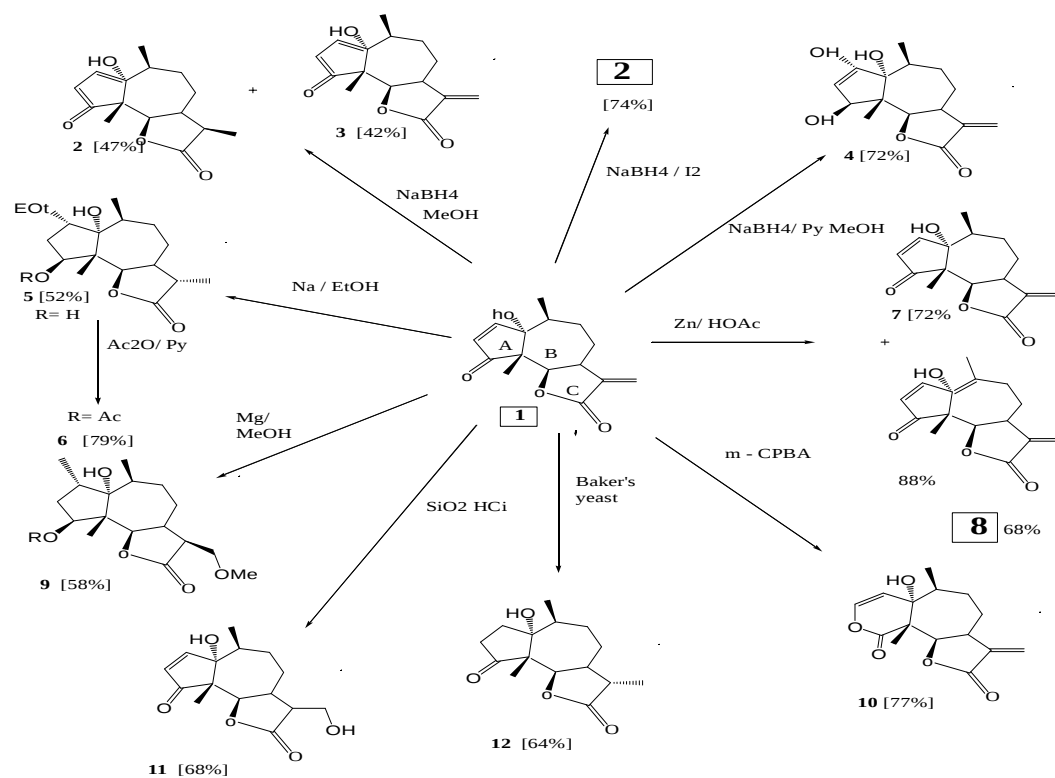
Parthenin (a sesquiterpene lactone) is a major constituent of *parthenium hysterophorus* –a noxious weed known for its environmental and health hazardous properties. . It is responsible for imparting the several properties to this weed such as allelpathy, autotoxicity and allergency. Further, anticancerous, antiameobic and antimalarial properties of the weed are also credited to parthenin. The greater quantity of Parthenin has been found to be responsible for livestock poisoning. The present review comprises the phytochemical biological reports of parthenin.. The future scope of the compound has been emphasized with a view to obtain structurally modified derivatives from parthenin so that these derivatives or bioactive moieties could be used for multifarious biological activities.

Keywords: parthenin; anticancerous; antiameobic; antimalarial; allelpathy.

INTRODUCTION

Parthenin (a sesquiterpene lactone) is a major constituent of *parthenium hysterophorus* –a noxious weed known for its environmental and health hazardous properties (Rodriquez et al.,1971; Towers et al.,1977) Parthenium hysterophorus is widely distributed throughout the tropics, occurring primarily in areas disturbed by man (Towers et al.,1977). According to Rollins (1950), the species is native to the region around the Gulf of Maxico, West Indies and Argetina. In Australia it was first recorded in Queens land in 1955, then it was eradicated but accidentally re-introduced again in 1958 (Haseter, 1976). In India Parthenium hysterophorus was first reported in 1956 from Pune (Rao et al., 1956).. The detrimental properties of Parthenium hysterophorus have been attributed mainly to the presence of a particular sesquiterpene lactone, Parthenin. It has been reported to be present in almost every part of the weed but is

concentrated more in the trichomes (Kanchan,1975) . It is responsible for imparting the several properties to this weed such as allelpathy(Kanchan and Jayachandra., 1979; Kanchan and Jayachandra.,1980) autotoxicity (Pichman and Pichman., 1984) and allergency (Mitchell et al.,1972) . Further, anticancerous (Mew et al., 1982), Antiameobic (Sharma and Bhutani.,1988) and antimalarial properties (Hopper et al., 1990) of the weed are also credited to parthenin. The greater quantity of Parthenin has been found to be responsible for livestock poisoning (Narasimhan et al., 1984; Pichman and Pichman.,1984). Several analogues of parthenin have been prepared in order to obtain different bioactive derivatives. The reduction of parthenin (Figure 1) was carried out with various readily available reducing agents including NaBH₄, NaBH₄/I₂, Na/EtOH, Mg/MeOH and Zn/HOAc (Das et al.,1999)



Scheme 1 : Reactions of Parthenin

Fig. 1: Reactions of parthenin with different chemicals

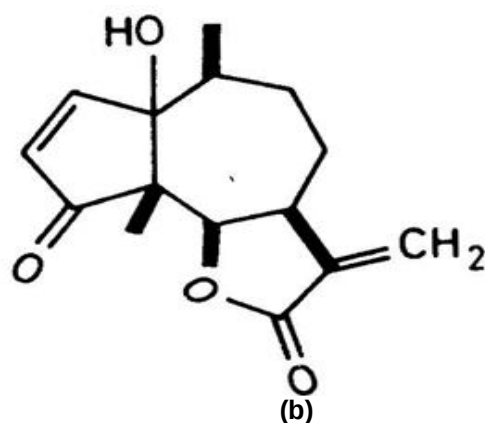
Biological activities of sesquiterpene lactones

Sesquiterpene lactones exhibit a variety of activities against different types of organisms. The major findings of individual types of biological activities of these compounds especially parthenin are summarized below.

Furthermore, the structure of these sesquiterpene lactones is responsible for their different types of biological activities. The structure of parthenin along with the plant from which it was obtained is shown as follows (Figure 2).



(a)



(b)

Fig. 2: (a) *Parthenium hysterophorus*; (b) Sesquiterpene lactone parthenin obtained from *Parthenium hysterophorus*

The major findings of individual types of biological activities of parthenin are as follows.

Antimicrobial activity

Most of the sesquiterpene lactones including parthenin has been reported to inhibit growth of bacteria and/or fungi (Olechmnowicz-Stepien and stepien., 1963; Vichkanova et al., 1971; Vanhaelen-Fastre., 1968, 1972; Mathur et al., 1975; Norman et al., 1976; Lee et al., 1977b; Towers et al., 1977a). It has been suggested (Lee et al., 1974, 1977b) that the unsubstituted cyclopentenone ring is a prerequisite for antimicrobial activity of sesquiterpene lactones, and that it is independent on the presence or absence of the α -methylene- γ -lactone moiety.

Allelopathic activity

Parthenium hysterophorus, a hazardous widespread weed that has infested agricultural lands in many parts of India and Australia, causes a serious reduction of many economically important crop species. The growth and yield of several crop species were considerably affected when they were grown in soil containing dried root and leaf materials of this weed (Kanchan and Jayachandra., 1976). These authors also observed that dried plant material or aqueous extracts from roots of *P. hysterophorus* caused a suppression in the growth and colonization of *Rhizobia* in leguminous plants. Parthenin and water extracts of *P. hysterophorus* inhibited seed germination and growth of seedlings of *Phaseolus vulgaris* (Garciduenas et al., 1972) wheat, and ragi (*Eleusine Coracana*) (Kanchan, 1975). In the later work almost all fractions of extracts showed inhibitory activity. On the basis of these and other data it has been suggested that *P. hysterophorus* contains a complex of inhibitors with parthenin and some phenolic acids as the prominent constituents (Kanchan, 1975; Kanchan and Jayachandra, 1976).

Effect on the insects

Parthenin from *P. hysterophorus* inhibits heart beat of grasshopper most likely by blocking thiol containing compounds important for normal heart activity. This is indicated by the fact that the activity of parthenin –arrested hearts can be restored by thiol addition (Picman et al., 1981).

Effect on mammals

Parthenin hysterophorus, when fed to cattle and buffaloes in excess quantity, was found to cause illness or death of the animals, most likely because of parthenin present in this

species (Narashimhan et al., 1977). The extract *P. hysterophorus* from which parthenin and other sesquiterpene lactones were removed could be used as a protein rich fodder (Savangihar and Jhosi., 1978), clearly showing that sesquiterpene lactones are responsible for the poisoning action of this plant.

Allergic contact dermatitis

Allergic contact dermatitis due to parthenin develops from repeated contacts with this plant or possibly with its disseminated trichomes and dried plant parts (Lonkar et al., 1974). It has been established that the exomethylene on the lactone ring is responsible for allergenicity of sesquiterpene lactones, however, this group alone is not always immunologically sufficient (Mitchell et al., 1970, 1971a,b; Mitchell and Dupuis., 1971; Epstein et al., 1980). Since parthenin undergoes a reaction with cysteine via the exomethylene on the lactone ring as well as via the C2-C3 double bond (Picman et al., 1979). The presence of these two active sites in a molecule of parthenin could be responsible for its strong allergenicity.

Cytotoxic activities

Sesquiterpene lactones are of great interest in cancer research because many of these compounds exhibit antileukemic, cytotoxic and/or tumor inhibitory activity. The relationship between chemical structure of sesquiterpene lactones and their cytotoxic activity was investigated by many researchers. In their review of antineoplastic agents of plant origin, Hartwell and Abbott (1969) concluded that all known active sesquiterpene lactones possess an α,β -unsaturated lactone ring. Later it was established that the conjugated exomethylene group on the lactone is an essential requisite for cytotoxicity (Kupchan, 1970; Kupchan et al., 1970, 1971).

Mutagenic activities

Parthenin, a sesquiterpene lactone from *P. hysterophorus*, has been reported to have the ability to break human leucocyte chromosomes in vitro and to induce micronuclei formation in the polychromatic erythrocytes of mice in vivo (Vaidya et al., 1978). The exact mechanism underlying the observed cytogenetic damage caused by parthenin is not known.

Anti-inflammatory activities

Hall et al. (1979) tested some sesquiterpene lactones for anti-inflammatory activities in the rodents. In the carrageenan inflammation

screening tests and in the tests for the inhibition of the writhing reflex, the exomethylene on the lactone ring of the sesquiterpene lactones was found to be required for potency.

Anti-malarial activity

Parthenin and some of its derivatives have been shown to possess significant anti-malarial activity against a multi-drug resistant strain of 'Plasmodium falciparum'. The activity of parthenin and its derivatives against malarial parasite may be due to their differential effects on host and Plasmodium membranes. (Hooper et al., 1990)

CONCLUSION

This study attempts to highlight the therapeutic potential of sesquiterpene lactone parthenin in the prevention or therapy of disease. From this study we can conclude that the results reviewed in the study are aimed at attracting the attention of researchers seeking new drugs from parthenin and its chemical derivatives, which can hopefully be considered in future for more clinical evaluations and possible applications and as adjuvant to current medications. We should maintain our efforts in considering and valorizing our natural patrimony as well as conducting more research on these sesquiterpene lactones and their pharmacological aspects.

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