

Recent results in the search for bioactive compounds from Turkish medicinal plants

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Abstract: During the past few years, some of the selected Turkish medicinal plant extracts have been screened for their antibacterial, antifungal, antiinflammatory, analgesic, anti-platelet and antihypertensive activities. Bioassay-directed fractionation using different pharmacological tests with the extracts from *Fumaria vaillantii*, *Fritillaria imperialis*, *Veratrum album*, *Symphytum officinale* and *Paeonia daurica* has led to the determination of different bioactive compounds. Data will be presented on the above aspects with crude extracts, fractions as well as pure compounds. The structures of new bioactive compounds will be reviewed.

INTRODUCTION

There is no doubt that plants are a good source of biologically active natural products. Plants contain too many useless compounds and the phytochemical approach is too wasteful of time and resources. The complete extraction of products from plant material is rarely achieved using classical methods of extraction and the separation of individual compounds from these extracts is frequently very difficult. In the investigation of bioactive natural compounds, it is essential to have access to simple biological tests to locate required activities. Therefore, extracts must be screened for biological activity, the active extracts selected, fractionations directed with bioassays and the bioactive compounds identified. In recent years, a more systematic approach to the discovery of drugs from Turkish medicinal plants has been initiated using bioassay-directed fractionation.

RESULTS

Many of the Turkish plants are known for their therapeutic properties and used in folk medicine in the treatment of a wide variety of diseases. However, these plants should be evaluated by modern scientific methods in order to prove their usefulness and to stop the use of toxic and useless plants. For this purpose, the following screening tests have been initiated for some Turkish medicinal plants.

Screening for Antibacterial Activity

Some plants traditionally used to prevent sepsis, which means that they have antibacterial activity. In order to determine their scientific basis for their use, the antibacterial effects of 102 plants were screened against eight bacteria by using the disc diffusion method. Aqueous and ethanolic extracts of these plants collected from different localities in Turkey were found to inhibit the growth of some Gram positive and Gram negative bacteria. Among them 29 plants have shown significant antibacterial activity. The ethanolic extracts were ascertained to be more effective than the aqueous extracts in inhibiting bacterial growth(1).

During the past ten years, a large number of isoquinoline alkaloids were isolated from *Fumaria* and *Corydalis* species growing in Turkey(2-7). It was of interest to examine the in vitro antibacterial activity of some isoquinoline alkaloids. Thirty-two isoquinoline derivatives from Turkish *Fumaria* and *Corydalis* species against several bacteria using disc-plate to discover new aspects of the relationship between antibacterial activity and chemical structure of them. Among the isoquinoline derivatives examined, phthalideisoquinolines and tetrahydroprotoberberines are the most active groups. The activity of protopines is similar to that of benzophenanthridines(8).

The antibacterial activity of triterpene saponins isolated from the roots of *Symphytum officinale* has also determined using agar diffusion method(9).

Screening for Antifungal Activity

In our continuing search for natural products, 102 plants were also investigated in the aspect of their antifungal activities(10). Their ethanolic extracts were tested against *Candida albicans* and three dermatophytes. Among these, 29 plant extracts have been found to possess higher activity than the others. The results indicate that the antifungal activities of these plant extracts might be related to their phenolic moieties.

Screening for Antiinflammatory Activity

Both steroidal and nonsteroidal antiinflammatory drugs currently used in the treatment of inflammatory diseases are known to have various side effects. Thus investigations for the new antiinflammatory agents with minimum side effects are still a challenge and studies on both synthetic drugs and plants are conducted to realize this purpose. In Turkish folk medicine, many plants have been used in the treatment of rheumatoid arthritis and some antiinflammatory diseases. The aqueous extracts of 29 plant species from 18 family were tested for their antiinflammatory activities by using carrageenan-induced hind paw edema method in mice. Ten of the plants showed significant antiinflammatory activity(11).

For the determination of active principle, the ethanolic extract of the roots of *Paeonia daurica* showed significant activity was subjected to a serial fractionation with hexane, chloroform, n-butanol and water, respectively. Each fraction was then tested for its antiinflammatory activity with carrageenan-induced hind paw edema method in mice. The hexane fraction was showed significant antiinflammatory activity. To determine the antiinflammatory principle of this fraction, two spots detected on tlc were separated with preparative tlc and each fraction was administered to mice. The active antiinflammatory principle was determined as paeonol. In order to find the amount of paeonol in this fraction, it was analyzed with HPLC and the paeonol content was calculated as 86.12 %. As a result of this study, the roots of *Paeonia daurica* could be used as a substitute for the official drug known as the roots of *Paeonia moutan* in traditional Chinese medicine(12).

Screening for Analgesic Activity

Analgesic drugs currently used are either narcotic or non-narcotics which have proven side and toxic effects. To develop new synthetic compounds in this category is an expensive and again may have some problems of side effects. On the contrary, many medicines of plant origin had been used and are in use successfully since long time without any serious effects. The lack of potent analgesic drugs now actually in use prompted this study in which some Turkish medicinal plants for their analgesic activities were screened by tail flick method in mice. The analgesic activities of these extracts were compared with acetylsalicylic acid used as standard drug. The results showed that the plants possessed varying degrees of analgesic activity at various doses(13).

Screening for Anti-platelet Activity

The role of anti-platelet drugs in the control of cardiovascular diseases continues to be emphasized. It is well recognized that platelet-vessel wall interactions are important in the development of thrombosis and atherosclerosis. Thus, inhibition of platelet function may be a promising approach for the prevention of thrombosis. Although many agents have been reported to have *in vitro* anti-platelet effects, only few of them are clinically useful in antithrombotic therapy. Therefore, it is very important in searching for new anti-platelet drugs for this purpose. The effect of some Turkish medicinal plants against human platelet aggregation induced by AA, collagen and PAF have been examined. Our preliminary biological activity evaluation of an ethanolic extracts of *Fumaria vaillantii*, *Narcissus tazetta* ssp. *tazetta*, *Leucojum aestivum*, *Pancreaticum maritimum*, *Thermopsis turcica*, *Buxus longifolia*, *Fritillaria imperialis*, *Cistus laurifolius*, *Consolida hellespontica*, *Urtica dioica*, *Taxus baccata* and *Nitraria schoberi* were the most potent inhibitors with minimal effective concentrations. Among them, *Fumaria vaillantii* showed complete inhibition on platelet aggregation caused by AA and collagen inhibitors of thromboxane formation. Bioassay-guided fractionation of the ethanolic extract of *Fumaria vaillantii* resulted in the isolation of protopine. The ethanolic extract of *Narcissus tazetta* ssp. *tazetta* also showed strong anti-platelet effects on AA and collagen induced platelet aggregation. During bioassay-directed fractionation studies, the alkaloidal fraction of this plant was also effective. For the determination of active compounds from *Narcissus tazetta* ssp. *tazetta* and other plants is in progress. In the case of the vasorelaxing effects, *Narcissus tazetta* ssp. *tazetta* showed inhibition on the contraction of rat aorta caused by high potassium and norepinephrine. This predicts that ethanolic extract of this plant may contain calcium-channel blocking agents.

Our current research programme on alkaloid-containing plants has recently led to the isolation and structure elucidation of new along with several known alkaloids belonged to different skeletons. Among new alkaloids, jervinone and 1-hydroxy-5,6-dihydrojervine as well as known alkaloid O-acetyljervine from the rhizomes of *Veratrum album* exhibited antihypertensive effect in dose-dependent manner(14). On the other hand, a new triterpenoidal saponin of hederagenin named Symphytoxide-A has been isolated from the roots of *Symphytum officinale*. This compound also exhibited hypotensive activity in anaesthetized rats(15).

As a part of our phytochemical studies, a new steroidal base, ebeinone has been isolated from the bulbs of *Fritillaria imperialis* along with other known steroidal bases. Ebeinone exhibited anticholinergic activity in isolated tissue experiments. Ebeinone also completely blocked inhibitory responses of acetylcholine

In conclusion, it must be emphasized that new biologically active compounds can be essential not only for new therapies but also as starting materials for semi-synthetic drugs and as lead compounds for the development of synthetic medicines.

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