

DOCTORAL DISSERTATION ABSTRACTS

QUANTITATIVE DETERMINATION USING UV, IR SPECTROSCOPIC AND HPLC METHODS FOR CALCIUM CHANNEL BLOCKERS AND β -ADRENERGIC RECEPTOR BLOCKERS IN BINARY MIXTURES

Füsun GEDİL ÜSTÜN

Supervisor: Prof. Dr. Okan ATAY, Gazi University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry
06630 Etiler, Ankara-TURKEY

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Binary combinations of calcium channel blockers and β -adrenergic receptor blockers are widely used in the treatment of hypertension.

In this presented study, binary combinations of nifedipine with mefruside, acebutolol, atenolol and metoprolol tartarat were determined quantitatively. For these quantitative determinations, thin layer chromatography, UV spectroscopy (absorbance ratio and Vierordt methods) and high pressure liquid chromatography (HPLC) methods were applied. UV spectroscopy, IR spectroscopy and HPLC methods were also used for medications containing active substance of 1,4-dihydropyridine derivatives (nifedipine, nimodipine, nisoldipine, nitrendipine and amlodipine).

The results of analysis using the mentioned methods were evaluated statistically and these methods were compared with respect to their sensitivity.

It has been shown that the methods used are alternative techniques in determination of commercial preparations that contain 1,4-dihydropyridine derivatives alone or in combination with a β -adrenergic receptor blocker.

Key Words: Calcium channel blockers, β -adrenergic receptor blockers, UV spectroscopy (absorbance ratio and Vierordt methods), IR spectroscopy, HPLC method, quantitative determination.

PHARMACOGNOSTICAL RESEARCHES ON SOME *VERBASCUM* SPECIES

İffet İrem TATLI

Supervisor: Prof. Dr. Zeliha Şükran AKDEMİR, Hacettepe University, Faculty of Pharmacy, Department of Pharmacognosy, 06100 Sıhhiye, Ankara-TURKEY

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The genus *Verbascum* is represented by 228 species, 185 of which are endemic in Turkish flora. The genus is classified into 13 groups (Groups A-M). In this study, three *Verbascum* species from three different groups among the 13 [*Verbascum pterocalycinum* var. *mutense* (Group C), *V. cilicicum* (Group F) ve *V. salviifolium* (Group K)] were researched from the point of view of their chemical constituents by means of phytochemical investigations of their overground parts. The air dried and powdered overground parts of the plants were extracted with methanol. The methanolic extracts of *V. pterocalycinum* var. *mutense* and *V. cilicicum* were used. After evaporation of the obtained methanolic extract of *V. salviifolium* under vacuum and low temperature, the crude extract was dissolved in water and extracted with chloroform, and the remaining water-soluble parts were used. By means of serial chromatographic study (open column chromatography, vacuum-liquid chromatography and middle-pressure liquid chromatography) of the extracts of *V. pterocalycinum* var. *mutense*, *V. cilicicum* and *V. salviifolium*, 2 saponins (ilwensisaponin A= mimengoside A; **VPM-1**, ilwensisaponin C; **VPM-2**), 2 iridoid glucosides (ajugol; **VPM-3**, picoside IV; **VPM-4**), a phenylethanoid glycoside (verbascoside= acteoside; **VPM-5**) and a monoterpene glucoside [1-(β -D-glucopyranosyl)-8-hydroxy-3,7-dimethyl-oct-2(*E*), 6(*E*)-dienoate; **VPM-6**] from *Verbascum pterocalycinum* var. *mutense*; 6 iridoid glycosides [catalpol; **VC-1**, verbaspinoside; **VC-2**, 6-*O*-(3"-*O*-*trans*-cinnamoyl)- α -L-rhamnopyranosyl-catalpol; **VC-3**, 6-*O*-(4"-*O*-*trans*-cinnamoyl)- α -L-rhamnopyranosylcatalpol; **VC-4**, saccatoside; **VC-5**, 6-*O*-(3"-*O*-*trans*-*p*-coumaroyl)- α -L-rhamnopyranosylcatalpol; **VC-6**] from *Verbascum cilicicum*; 4

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phenylethanoid glycosides (β -hydroxyacteoside; **VS-2**, forsythoside B; **VS-3**, angoroside A; **VS-4**, martynoside; **VS-5**), 2 neolignan glucosides (dehydrodiconiferyl alcohol-9'-*O*- β -D-glucopyranoside; **VS-1a**, dehydrodiconiferyl alcohol-9-*O*- β -D-glucopyranoside; **VS-1b**) and 4 flavone glucosides (apigenin 7-*O*-glucoside; **VS-6**, luteolin 7-*O*-glucoside; **VS-7**, chrysoeriol 7-*O*-glucoside; **VS-8**, luteolin 3'-*O*-glucoside; **VS-9**) from *Verbascum salviifolium* were isolated. The structures of the isolated compounds were elucidated by means of spectroscopic (IR, UV, $^1\text{H-NMR}$, $^{13}\text{C-NMR}$, 2D-NMR and mass spectroscopy) evidence. Radical scavenging activity of the methanol extracts prepared from the plant specimens and the compounds isolated were tested towards the 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical in the TLC system. In our continuing studies, the inhibition on DPPH radical of the phenolic compounds was measured spectrophotometrically. The phenylethanoid, neolignan and flavone glycosides (**VPM-5**, **VS-2**, **VS-3**, **VS-4**, **VS-5**, **VS-1a**, **VS-1b**, **VS-6**, **VS-7**, **VS-8**, **VS-9**) demonstrated a strong scavenging activity. On the other hand, the inhibition of reactive oxygen species within cancer cell lines by the isolated compounds was determined flow-cytometrically. Ilwensisaponin A and C, verbascoside, β -hydroxyacteoside, forsythoside B, angoroside A, martynoside, apigenin 7-*O*-glucoside, luteolin 7-*O*-glucoside, chrysoeriol 7-*O*-glucoside, and luteolin 3'-*O*-glucoside showed a strong activity. To determine the effects on inflammation, the isolated compounds were also evaluated for their inhibition of aggregation and adhesion of cancer cell lines. Ilwensisaponin A and C as well as verbascoside demonstrated a strong activity. A brief chemotaxonomical discussion by means of a comparison of the title plants from the point of view of their chemical constituents was also given.

Key Words: *Verbascum pterocalycinum* var. *mutense*, *Verbascum cilicicum*, *Verbascum salviifolium*, Scrophulariaceae, saponins, iridoid glycosides, phenylethanoid glycosides, neolignan glucosides, flavone glucosides, monoterpene glucoside, free radical scavenging property (antioxidant activity), antiinflammatory activity, chemotaxonomy.