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## Evaluation of anti-inflammatory action of *Primula veris* L.

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### Abstract

Eight extracts of *Primula veris* L. leaves and underground organs in different doses (50, 100, 150 and 200 mg/kg) were evaluated for their anti-inflammatory activity against carrageenan-induced paw edema in rats and compared with sodium diclofenac. The result indicated that thick extracts of both parts of cowslip proved to be the most effective in the dose 200 mg/kg. Thick extract of *Primula veris* leaves exhibits the greatest inhibition activity against mentioned edema.

**Keywords:** *Primula veris*, anti-inflammatory action, thick extract

### 1. Introduction

Cowslip primrose or cowslip (*Primula veris* L.) is a herbaceous perennial flowering plant with a rosette of leaves and yellow flowers in clusters on a single stem. This plant is widely distributed throughout Europe with Bulgaria and Turkey the principal commercial sources as well as central and western Asia in sunny meadows and light underbrush [1, 2]. Cowslip has long been known in folk and later in the traditional medicine for its healing properties. Herbal medicine has used the leaves, flowers and rhizomes with roots of cowslip as expectorant, diuretic, analgesic, antirheumatic, sedative and antispasmodic remedy [3]. Leaves of this plant contain a significant amount of vitamin C and are applied in avitaminosis or hypovitaminosis. Infusion from cowslip leaves can be recommended in gout, kidney and bladder complaints. Infusion from flowers has often been used to treat common cold and flu-like symptoms, throat and lungs inflammation; for headaches including migraines. The antispasmodic property of cowslip makes it useful in treating epilepsy and tremors. Medicines from flowers are mild sedatives and are applied to calm and help sleeping [1].

In traditional medicine cowslip roots are used as expectorant for the treatment of bronchial conditions.

The results of our preliminary research revealed the high content of phenolic substances in leaves and rhizomes with roots from *P. veris* L. Content of tannic substances was 1.23 % and 1.74 % respectively; flavonoids – 8.26 % and 0.48 % respectively; hydrocinnamic acids – 2.71 % and 1.99 % respectively. Amount of simple phenols in leaves reached 3.63 % and in roots – 3.95 % [4-6]. The analyzed plant also contains volatile oils. According to many references all these substances possess anti-inflammatory effect [7, 8] and thus the aim of our study was to comparatively evaluate the anti-inflammatory action of leaves and rhizomes with roots of *P. veris* L. using carrageenan-induced paw edema in rat.

### 2. Materials and Methods

#### 2.1 Plant material and chemicals

The leaves of *P. veris* L. were collected in Ternopil region (Ukraine) in the flowering period in April-May 2015. The subterranean organs were collected in September-October, after dying of aboveground part. The selected parts of these plants were then dried under the shade, then chopped, grounded and stored at paper bags.

The extraction was performed by maceration technique using 40 % alcohol solution as solvent.  $\lambda$ -carrageenan was purchased from Sigma Chemical Company, USA. Diclofenac sodium was manufactured by Public joint-stock company "CPP the "Red star" (Kharkiv, Ukraine).

#### 2.2 The carrageenan-induced rat paw edema

The research of extracts was conducted on 70 adult Wistar albino male rats (180-200 g) obtained from Institute of Pharmacology and Toxicology of the Academy of Medical Sciences of Ukraine. Rats were maintained at vivarium of National Pirogov Memorial Medical University in standard conditions and allowed free access to food and drinking water. Lighting was provided for 12 hours.

All animal experiments were carried out in accordance with the Council Directive 86/609/EEC of 24 November 1986 on the approximation of laws, regulations and administrative provisions of the Member States regarding the protection of animals used for experimental and other scientific purposes [9]. The protocol of the study was approved by the Ethics Committee of the National Pirogov Memorial Medical University, Vinnytsia.

The carrageenan-induced rat paw edema was used for the introduction of inflammation. Method was reproduced by subplantar injection of 0.1 ml 1 % carrageenan solution into right hind paw of each rat [10]. Thick extracts of *P. veris* leaves (50, 100, 150 and 200 mg/kg) thick extract of *P. veris* rhizomes and roots (50, 100, 150 and 200 mg/kg) and diclofenac sodium (8 mg/kg, the ED50 of mentioned model of pathological process) were intraperitoneally administered 1 hour before the carrageenan injection. The paw volume of rats was measured by the plethysmometer at the 3<sup>rd</sup> hour of inflammation (the peak of inflammation).

The anti-inflammatory effect of analyzed extracts was calculated by the following equation and compared to control animals injected the equivalent volume of solvent:

$$X = \frac{100\% - (V_1 - V_2) \times 100}{V_{1contr} - V_{2contr}}$$

Where,

$V_1$  – volume of inflamed paw in experiment;  
 $V_2$  – volume of normal paw in experiment;  
 $V_{1contr}$  – volume of inflamed paw in control test;  
 $V_{2contr}$  – volume of normal paw in control test.

### 2.3 Statistical analysis

Statistical processing of the study results was conducted using variation statistic methods with computer statistic package programs Statistica 8.0 (StatSoft inc., USA), the nonparametric Mann–Whitney U test and Kruskal-Wallis test. Value of  $p < 0.05$  was considered to be significant. The value of studied parameters are presented as  $M \pm m$ , where  $M$  – arithmetic mean value,  $m$  – standard error of the mean.

### 3. Results and Discussion

Results of our research revealed the antiexudative action in carrageenan rat paw edema for extracts from leaves and rhizomes with roots of cowslip in all doses. Treatment with cowslip thick extracts reduced the paw edema in a dose-dependent manner (see Table 1). Various studies suggest that antiexudative action of some substances on carrageenan-induced edema proves the effect of mentioned substance on kinin system, histamine and prostaglandines produced by cyclooxygenase enzymes (COX) in early stage of inflammation. COX initiates the synthesis of prostaglandines and this leads to inflammation, lithogenesis, cell proliferation and destruction [12, 13].

**Table 1:** The effect of *Primula veris* L. thick extracts on paw volume of rats in comparison with diclofenac sodium ( $M \pm m$ ,  $n=7$ )

№	Substance	Dose mg/kg	Volume of inflamed paw (mm <sup>3</sup> )	Volume of normal paw (mm <sup>3</sup> )	Increase (%)	Antiexudative action, %
1	Control pathology (1 % carrageenan solution)	-	534,8±27,1*	255,5±63,6	121,0	0
2	PLTE	50 mg/kg	562,5±34,2*	311,0±34,6	82,3	9,9
3	PLTE	100 mg/kg	547,2±42,9*	310,0±31,3	76,9	15,1
4	PLTE	150 mg/kg	539,3±31,9*	341,9±31,2	58,4	29,3
5	PLTE	200 mg/kg	462,8±41,7#	287,5±22,5	61,0	37,2
6	PRRTE	50 mg/kg	526,4±35,6*	276,4±22,2	90,8	10,5
7	PRRTE	100 mg/kg	504,9± 57,4*	275,4± 45,0	85,0	17,8
8	PRRTE	150 mg/kg	523,1±43,0*	305,9±27,3	71,2	22,2
9	PRRTE	200 mg/kg	541,5±57,8*	343,9±60,6	59,5	29,1
10	Diclofenac sodium	8 mg/kg	502,43±27,9#	403,5±21,4	24,6	64,6

Notes:

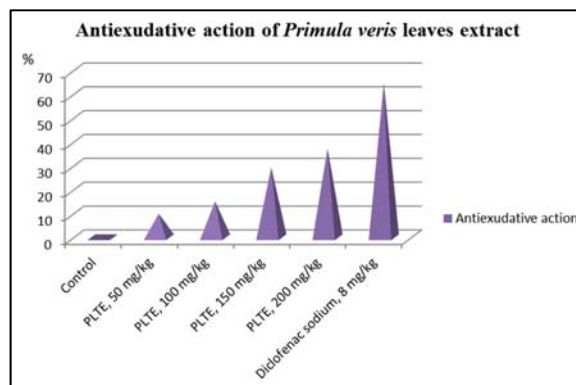
PLTE – thick extract of *Primula veris* leaves

PRRTE – thick extract of *Primula veris* rhizomes and roots

\* - significant difference ( $p < 0, 05$ ) between normal and inflamed rat paw

# - significant difference ( $p < 0, 05$ ) compared with control

According to the table above the most pronounced anti-inflammatory effect was recorded for cowslip extracts from leaves. The highest level of antiexudative action on carrageenan-induced paw edema in rats for mentioned above extract was in dose 200 mg/kg – 37.2%. This extract was only 1.7 times smaller than diclofenac sodium (64.6%) for desirable effect (see Table 1, fig. 1).



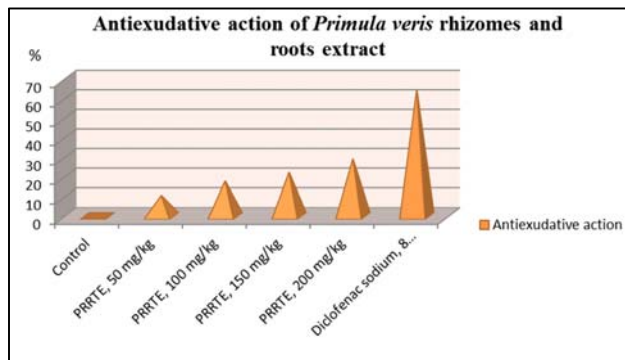
**Fig 1:** Antiexudative action of thick extract from *Primula veris* L. leaves on carrageenan-induced rat paw edema ( $n=7$ )

Notes:

PLTE – thick extract of *P. veris* leaves

PRRTE – thick extract of *P. veris* rhizomes and roots

Thick extract from cowslip rhizomes and roots showed less pronounced effect (see Table 1, Fig. 2). Extract from subterranean organs had the highest antiexudative action in the highest dose – 200 mg/kg, but it was 1.3 times lower than that of thick extract from leaves and 2.2 times lower than diclofenac sodium and was 29.1% (see Fig. 2).



**Fig 2:** Antiexudative action of thick extract from *Primula veris* L. rhizomes and roots on carrageenan-induced rat paw edema (n=7)

Notes:

PLTE – thick extract of *P. veris* leaves

PRRTE – thick extract of *P. veris* rhizomes and roots

Therefore, thick extract from *P. veris* L. leaves revealed that obtained from rhizomes and roots (see Fig. 1, Fig. 2).

#### 4. Conclusion

The anti-inflammatory effect of *P. veris* L. extracts from leaves and underground organs was proved on carrageenan-induced rat paw edema. The most desirable action of both types of extracts was at the dose level 200 mg/kg. Thick extract of primrose leaves possessed the most desirable effect and it was 37.2%. Our findings provide new perspectives on the therapeutic use of *P. veris* L leaves in the treatment of inflammatory diseases.

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