

## **Influence of moderate physical exertion on subacute low back pain, after *Symphytum officinale* ointment treatment** **Influența efortului fizic moderat asupra durerii lombare subacute, după tratamentul cu un unguent conținând *Symphytum officinale***

**Ramona Jurcău<sup>1</sup>, Ioana Jurcău<sup>2</sup>**

<sup>1</sup>*"Iuliu Hațieganu" University of Medicine and Pharmacy, Cluj-Napoca*

<sup>2</sup>*Pediatric Clinical Hospital, Cluj-Napoca*

### **Abstract**

*Background.* Lumbar pain has a medical, psycho-emotional and social importance. At present, more accent is placed on pain phytotherapy. Of plants, *Symphytum officinale* (SO) is known for its anti-inflammatory and analgesic actions.

*Aims.* The objective of the study is to monitor the influence of moderate physical exertion on some sedentary subjects with subacute low back pain, after their treatment with a phytotherapeutic ointment containing SO (PSO), compared with non-treated control subjects.

*Methods.* The chosen subjects (n=30) were selected based on the requirements of the study. Exercise consisted of pedaling on the Stepper 130 rpm/0-999 W/RUN 7414-15-T, 8 days, 3 min/test/day, at a strength that was increased by 11 watts/day. The analyzed indicators were local pain sensation (P) and anxiety (A). The chosen phytotherapy preparation was PSO. Statistical evaluation was done based on the Student test.

*Results.* Following PSO administration, P decreased in the period prior to exercise, and P and A were significantly reduced during exercise, compared to the untreated group, at all testing times.

*Conclusions.* 1) At the end of PSO ointment therapy, both after the first and the second period of phytotherapeutic preparation use, the sensation of pain was significantly reduced in subjects with subacute lumbar pain. 2) The pain sensation and anxiety were significantly reduced in subjects treated with PSO ointment compared with untreated subjects, under moderate physical exertion conditions by pedaling on a stepper. 3) OSP ointment phytotherapy provided analgesic and emotional protection in the treated subjects, in moderate exercise by stepper pedaling. 4) Given the results obtained with the PSO ointment, as well as its therapeutic qualities of good tolerance by the body, absence of toxicity and economic accessibility, we propose its use by subjects with subacute low back pain, as a form of pain therapy and analgesic protection, during rest and under moderate exercise conditions.

**Key words:** lumbar pain, *Symphytum officinale*, pain, anxiety, VAS, STAI, moderate exercise, stepper.

### **Rezumat**

*Premize.* Durerea lombară are importanță medicală, psiho-emotională și socială. În prezent, se pune tot mai mult accent pe fitoterapia durerii. Dintre plante, *Symphytum officinale* (SO) este cunoscut pentru acțiunile sale antiinflamatorii și antialgice.

*Obiective.* Obiectivul studiului este monitorizarea influenței efortului fizic moderat, asupra unor subiecți sedentari, cu dureri lombare subacute, după tratarea lor cu un unguent fitoterapeutic cu conținut de SO (PSO), comparativ cu subiecți martor netratați.

*Metodă.* Subiecții aleși (n=31) au fost selectați conform cerințelor studiului. Efortul fizic a constat în pedalarea pe Stepper 130 rpm/0-999 W/RUN 7414-15-T, 8 zile, 3 min/testare/zi, la o rezistență crescută cu 11 watt/zi. Indicatorii analizați au fost senzația de durere locală (P) și starea de anxietate (A). Preparatul fitoterapeutic ales a fost PSO. Evaluarea statistică s-a făcut pe baza testului Student.

*Rezultate.* În urma administrării PSO, P a scăzut în perioada anterioară efortului fizic, iar pe durata acestuia, P și A au fost semnificativ reduse față de lotul netratat, la toate momentele testării.

*Concluzii.* 1) La sfârșitul terapiei cu PSO, P, atât după prima cât și după a doua sesiune de utilizare a preparatului ales, a fost semnificativ redusă la subiecții cu durere lombară subacută. 2) P și A au fost semnificativ diminuate la subiecții tratați cu PSO, comparativ cu cei netratați, în condițiile efortului fizic moderat de pedalare pe un stepper. 3) Terapia cu PSO a asigurat subiecților tratați protecția antialgică și a stării emoționale, în condițiile efortului fizic moderat ales. 4) Date fiind rezultatele obținute cu PSO unguent, precum și calitățile terapeutice, de bună tolerare de către organism, absența toxicității și accesibilitate economică, propunem folosirea lui de către subiecți cu dureri lombare subacute, ca terapie și protecție antialgică, în condiții de repaus și de efort fizic moderat.

**Cuvinte cheie:** durere lombară, *Symphytum officinale*, senzația de durere, anxietate, VAS, STAI, efort fizic moderat, stepper.

---

Received: 2013, June 16; Accepted for publication: 2013, July 22;

Address for correspondence: "Iuliu Hațieganu" University of Medicine and Pharmacy, Cluj-Napoca, 400012, Victor Babeș Str., no. 8

E-mail: ramona\_mj@yahoo.com

---

Copyright © 2010 by "Iuliu Hațieganu" University of Medicine and Pharmacy Publishing

**Introduction**

Pain is “an unpleasant sensory and emotional experience associated with actual or potential tissue damage” (Loeser & Treede, 2008). Fear of injury has been posited as crucial in pain-related anxiety and in the development of chronic pain (Thibodeau et al., 2013). Of the types of pain, low-back pain is a common condition and a substantial economic burden in industrialized societies (Gagnier et al., 2006). Chronic low back pain (CLBP) is a common, yet challenging condition for both patients and clinicians (Esteves et al., 2013). Regarding the importance of synthesis medication in pain, Bogduk said in 2004 the following (Bogduk, 2004): “On the basis of the evidence, no drug regimen can be legitimately recommended for back pain.” Also in 2004, Reisner stated that “pain therapies from natural sources date back thousands of years to the use of plant and animal extracts for a variety of painful conditions and injuries” (Reisner, 2004). “Before extraction and synthetic chemistry were invented, musculoskeletal complaints were treated with preparations from medicinal plants, either administered orally or topically” (Cameron & Chrubasik, 2013). It is known that *Symphytum officinale* (SO) “has been used over many centuries as a medicinal plant. In particular, the use of the root has a longstanding tradition” (Staiger, 2012; Staiger, 2013).

The present article is a continuation of previous research of the authors regarding the relationship between sport and stress (Jurcău et al., 2011; Jurcău et al., 2012b) and the modulation of anxiety in physical stress with herbs (Jurcău, 2012; Jurcău et al., 2012a) or other methods (Jurcău & Jurcău, 2012).

**Hypothesis**

Pain is a topic of concern in medical research, and low back pain has been the object of numerous studies. Phytotherapeutic influence on pain, in general, and on low back pain, in particular, is a topic of permanent interest. Subacute low back pain has been less evaluated in terms of moderate exercise in subjects previously treated by phytotherapy.

**Objectives**

We intend to monitor the influence of moderate physical exertion, represented by pedaling on a stepper, on sedentary subjects with low back pain - after treating them with a phytotherapeutic ointment with a complex herbal content with synergistic action, including *Symphytum officinale* (PSO) - compared to sedentary subjects with the same kind of pain, but untreated, through the comparative evaluation of pain and anxiety.

**Material and methods**

We mention that - in conformity with the Helsinki Declaration, Amsterdam Treaty and Directive 86/609/EEC - we obtained the necessary license from the Ethics Commission of the College of Physicians, Cluj county, for our research on human subjects, and for the informed consent of the subjects included in the research.

The study and measurements were carried out during April-May 2013, in the Medical Family Office 122 in Cluj-Napoca.

a) *Groups*

The participation of all subjects in the study was voluntary. The subjects were tested on the Stepper 130 rpm/0-999 W/RUN 7414-15-T (3). We chose this type of equipment because its use leads to an important low back muscle exertion. The selected subjects were sedentary and diagnosed by the family doctor with subacute low back pain, due to prolonged sitting position at work, without other pathological correlations. Subjects with low back pain other than the selected one, mental disorders, antiinflammatory, antalgic or cortisone therapies and toxic addictions - alcohol, tobacco, drugs, coffee were excluded from the study.

Two groups were explored: the control group (C) that received no therapy and the experimental group (E), which was administered PSO. Both groups were subjected to the same type of physical exercise on the stepper.

b) *Subjects*

The number of subjects by groups was 12 women for E and 19 women for C. The mean age was 30.2±3 for E and 32.4±4 for C (Table I). The participants were asked not to consume alcohol, coffee, not to smoke and not to use any medication or antioxidant during the moderate physical exercise study.

**Table I**

The number and type of subjects by groups.

Group	Experimental stress (E)	Control (C)
No. of subjects	12	19
Mean age	28.2 ± 3	31.4 ± 4
Gender	women	women

c) *Study design*

As a model of moderate physical exertion, exercise conducted on the Stepper 130 rpm/0-999 W/RUN 7414-15-T was chosen. The exercise testing method was the following: total duration of test = 8 days; duration/testing/day = 3 minutes/testing/day, in the morning between 8.00-10.00 hours; the type of exercise = stepping on the pedal, at a rate of 80 steps/minute; resistance in watts/testing/day increased by 11 watts/day compared to the previous day, from 21 watts on the first day to 98 watts on the last day.

The chosen phytotherapeutic preparation has a particular content of *Comfrey* = *Symphytum officinale* (PSO) and is called “Artrin” (1, 2). We chose it for its qualities: antiinflammatory and antalgic effects, good tolerance by the body, absence of toxicity and economic accessibility. PSO was administered to E before the beginning of exercise on the stepper, daily, over two periods of three weeks each, with a one-week break between the two periods, as follows: local application on the previously cleaned lumbosacral area, at 7.00, 12.00, 17.00 and 20.00 hours.

d) *The indicator determination program* was the same for C and E, being carried out as follows:

- The treatment period: time 1 = first time determination, basal (T1) - on the day prior to the start of the first period of PSO treatment, in the morning; time 2 = (T2) - on the day prior to the start of the second period of PSO treatment, in the morning.

- The physical exertion period: times 3-6 = (T3-T6) - on

each of the days 1, 3, 6, 8, immediately before exercise - for A, and immediately after exercise - for P.

e) *Explorations*

The examinations consisted of measuring pain and anxiety

- *Local pain assessment (P)*

It was performed by determining the pain score using the Visual Analogue Scale, which is a 10 cm horizontal line anchored at both ends, with the left end anchor (i.e. 1 cm) representing the minimum score (without pain) and the right end anchor (i.e. 10 cm) representing the maximum score (maximum pain). Each patient was asked to rate her pain by means of a vertical mark, which intersects the Visual Analogue Scale line at an appropriate point, under the rules of use of this scale (Scott & Huskisson, 1976; Reips, 2008).

- *Psychological anxiety assessment (A)*

The self-assessment questionnaire, STAI X1, X2 (State-Trait Anxiety Inventory) was used for anxiety (A) (Spielberger, 1983). STAI scores range from a minimum score of 20 to a maximum score of 80 on both A - State and A - Trait scales. Subjects respond to each item of STAI, by assessing themselves on a 4-point Likert scale (Jurcau et al., 2011; Jurcau et al., 2012a). The A - State scale is balanced with 10 directly quoted items and 10 (reverse scored) items; the reverse scored items of the A - State scale are: 1, 2, 5, 8, 10, 11, 15, 16, 19, 20. The A - Trait scale has 13 directly quoted items and 7 reverse scored items, in which case it is not possible to have a fully balanced scale; the reverse scored items of the A - Trait scale are: 1, 6, 7, 10, 13, 16, 19. The psychometric properties of STAI are good, with a Cronbach  $\alpha$  (Cronbach, 1951, 2004) of 0.84, higher than the conventional cut-off value of 0.70.

f) *Statistical evaluation*

- The results obtained were analyzed using the SPSS 13.0. statistical package.

- For continuous data examination, Student's t test was used.

- The differences were considered significant at a  $p < 0.05$ .

**Results**

Note that the *reference values* were those of C and the *reference time* was considered to be T<sub>1</sub>.

a) *Pain* (Fig.1). For C, P values were increased at T1; P values were insignificantly increased from T1 to T2 and T3 and significantly increased from T1 to T4 ( $p < 0.03$ ), T5 ( $p < 0.01$ ) and T6. For E, P values were increased at T1; compared to T1, P values were significantly lower at T2 ( $p < 0.03$ ), T3 ( $p < 0.005$ ) and T4 ( $p < 0.05$ ), and they were insignificantly lower at T5 and T6. With the exception of T1, when P values were similar, at all assessment times, P values for C were higher than for E, with significant differences at T2 ( $p < 0.05$ ), T3 ( $p < 0.02$ ), T4 ( $p < 0.01$ ), T5 ( $p < 0.005$ ), and T6 ( $p < 0.004$ ).

**Table II**

Impact of PSO therapy on pain.

Evaluation time	C - VAS		E - VAS	
	Arithmetic mean	Standard deviation	Arithmetic mean	Standard deviation
T1	4.4	± 2.823	4.2	± 2.411
T2	4.3	± 2.418	3.1	± 1.903
T3	4.4	± 2.992	2.1	± 1.023
T4	5.1	± 3.192	2.6	± 1.331
T5	6.6	± 4.128	3.1	± 1.813
T6	8.4	± 6.002	3.9	± 2.024

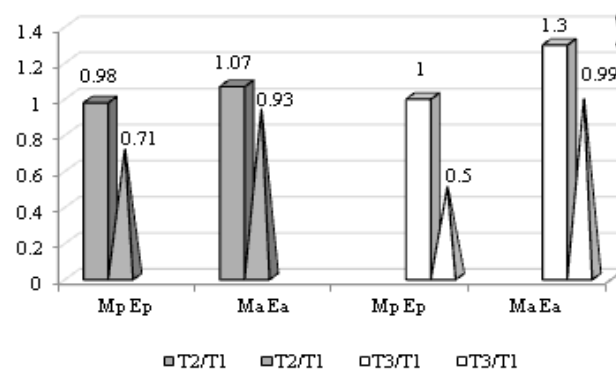
b) *Anxiety* (Fig. 2). For C, A values were unchanged from T1 to T2 and were significantly increased from T1 to T3 ( $p < 0.05$ ), T4 ( $p < 0.04$ ), T5 ( $p < 0.01$ ), and T6 ( $p < 0.003$ ). For E, A values compared to T<sub>1</sub> were unchanged at T2 and T3, insignificantly increased from T1 to T4 and T5 and slightly significantly increased from T1 to T6 ( $p < 0.05$ ). At all assessment times, A values for C were higher than for E, with significant differences at T3 ( $p < 0.05$ ), T4 ( $p < 0.01$ ), T5 ( $p < 0.003$ ), and T6 ( $p < 0.004$ ).

**Table III**

Impact of PSO therapy on anxiety.

Evaluation time	C - STAI		E - STAI	
	Arithmetic mean	Standard deviation	Arithmetic mean	Standard deviation
T1	28.2	± 4.314	28.5	± 5.412
T2	30.1	± 8.022	26.4	± 4.404
T3	36.8	± 10.201	28.3	± 6.024
T4	45.4	± 12.415	32.3	± 9.391
T5	56.6	± 13.904	40.2	± 10.131
T6	69.6	± 19.412	48.1	± 12.306

c) *The evaluation of PSO modulation on the analyzed parameters at times T2 and T3 compared to T1* shows the impact of PSO therapy on the evaluated values of the parameters, in E compared to C, after the first PSO treatment period, and after the second PSO treatment period, compared with T1. Thus, the most important PSO influence is on pain sensation, in E, at T3 (0.5).



**Fig. 3** - Impact of PSO therapy on P and A, at T2 and T3 compared to T<sub>1</sub>.

Groups:

Cp = Control - P, Ca = Control - A

Ep = Experimental - P, Ea = Experimental - A

!" = starting time for moderate exercise

d) The evaluation of PSO modulation on the analyzed parameters at time T6 compared to T1 shows the impact of PSO therapy on the evaluated values of the parameters, in E compared to C, at the maximum intensity time of moderately applied exercise, compared to the immediately post-PSO therapy time. Thus, the most important PSO influence is on pain sensation (1.07) and on anxiety (1.5) in E.

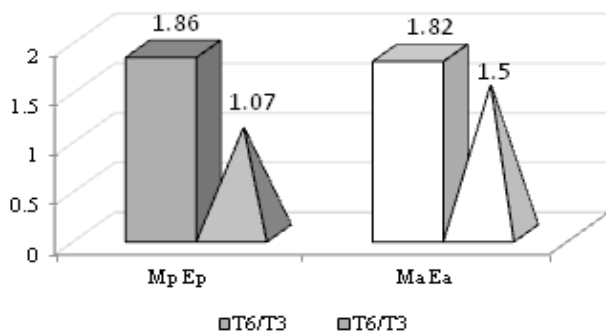


Fig. 4 - Impact of PSO therapy on P and A, at T6 compared to T3. Groups:

Cp = Control - P, Ca = Control - A  
 Ep = Experimental - P, Ea = Experimental - A  
 "!" = starting time for moderate exercise

## Discussion

In 2004, Bogduk stated the following regarding the importance of synthesis medication in pain (Bogduk, 2004): "Drugs constitute a convenient option for low back pain and are commonly used. However, evidence for their efficacy is meagre. Many drugs used for back pain are no more, or only slightly more, effective than placebos. Others have side effects that outweigh their usefulness in relieving pain. On the basis of the evidence, no drug regimen can be legitimately recommended for back pain".

### PSO and local pain sensation

Local PSO ointment application to E had the most significant results after the second PSO treatment period, which is evidenced by the significantly greater reduction in pain sensation from T1 to T3 ( $p < 0.005$ ), compared to the decrease from T1 to T2 ( $p < 0.03$ ).

By comparing the evolution of pain sensation for E and C throughout the study, it can be said that the chosen local PSO therapy provided protection against pain, which is demonstrated by the significant differences recorded with VAS for the non-physical exertion state (T2,  $p < 0.05$ ; T3,  $p < 0.02$ ), and especially for moderate physical exertion conditions (T4,  $p < 0.01$ ; T5,  $p < 0.005$  and T6,  $p < 0.004$ ), with the most important differences at intense physical exercise moments, T5 and T6.

### PSO and anxiety

Like in the other studies related to stress performed by us (Jurcău et al., 2011; Jurcău et al., 2012a; Jurcău & Jurcau, 2012), in this case too it was confirmed that changes in anxiety are anticipatory, values increasing for both C and E before physical exertion, which thus was proved to be perceived as a stress factor.

Although PSO does not have therapeutic indications

for anxiety modulation, we believe that in this E case, the reduction of anxiety might match with the decrease of fear regarding the possibility of pain appearance, along with the reduction of pain perception.

### Pain and *Symphytum officinale* SO - Recent studies

The antiinflammatory, antalgic and anti-contracture effects of SO are supported by a number of Pubmed publications, of which we mention some related to this topic.

SO has proved to be effective in various types of pain. Thus, its effectiveness in osteoarthritis, sprains, muscle pain is demonstrated by the following results: a) "active topical comfrey formulations were effective in relieving pain and stiffness and in improving physical functioning and were superior to placebo in those with primary osteoarthritis of the knee without serious adverse effects" (Smith & Jacobson, 2011); b) "the use of topical comfrey product in patients with acute ankle distortion decreased the scores for pain on active motion, pain at rest and functional impairment, amelioration of swellings and overall tolerability was excellent" (Kucera et al., 2004); c) "the data showed superiority of the comfrey extract based ointment over the diclofenac gel in the treatment of distortions of unilateral ankle sprains" (D'Anchise et al., 2007); d) "study results confirm the known anti-inflammatory and analgesic effects of topical *Symphytum* cream in the treatment of patients with myalgia" (Kucera et al., 2005); e) "comfrey root is a valuable and rational therapeutic option for patients suffering from muscles and joint pain" (Wurglics & Ude, 2012).

Three recent studies show the importance of SO in low back pain: a) "there was a significant treatment difference between comfrey extract and placebo – VAS pain intensity decreased on average (median) approximately 95.2%; comfrey root extract showed a remarkably potent and clinically relevant effect in reducing acute back pain; for the first time a fast-acting effect of the ointment (1 h) was also witnessed" (Giannetti et al., 2010); b) "multiple randomized controlled trials have demonstrated the efficacy and safety of comfrey preparations for the topical treatment of pain, inflammation and swelling of muscles and joints in degenerative arthritis, acute myalgia in the back, sprains, contusions and strains after sports injuries and accidents, also in children aged 3 or 4 and over" (Staiger, 2012); c) "this randomised, multicentre, double-blind, three-arm, placebo-controlled trial compared a topical combination of 35% comfrey root extract plus 1.2% methyl nicotinate versus a single preparation of methyl nicotinate or placebo cream for relief of acute upper or low back pain; they applied a 12 cm layer of cream three times daily for 5 days; VAS on active standardised movement was markedly smaller in the combination treatment group than in the methyl nicotinate and in the placebo group" (Pabst et al., 2013).

### Correlation between pain/ low back pain and anxiety - Recent studies

In 2012, Ellegaard and Pedersen claimed that "chronic low back pain (CLBP) is a stress factor in itself; when pain, stress and depression become overwhelming and there are few internal resources available, stress seems to become prominent." (Ellegaard & Pedersen, 2012).

Fear of injury directly predicts pain-related anxiety and indirectly predicts self-reported behavioral impairment; however, research has only measured fear of injury indirectly through other constructs (e.g., fear of illness and fear of movement) (Thibodeau et al., 2013). Regarding chronic low back pain (CLBP), in one of this year's studies Esteves mentions that: "Several studies have demonstrated a strong association between CLBP and psychological factors such as anxiety, fear-avoidance, self-efficacy, catastrophizing and depression. These factors are closely linked with emotional states; however, it is unknown whether CLBP patients process their emotions differently from asymptomatic individuals. The results suggest that dysfunctional emotional processing, particularly with regard to the suppression of emotions, is associated with CLBP" (Esteves et al., 2013). There is also recent evidence of this pain-emotional changes link, "in the present study we found compelling evidence for alterations of grey matter architecture in CLBP in brain regions playing a major role in pain modulation and control" (Ivo et al., 2013). Maybe this is why "psychological treatments have been successful in treating CLBP" (Domenech et al., 2013).

*The peculiarities of this study compared to cited results*

*Similarities:* a) the utility of SO as an anti-inflammatory ointment in osteoarticular and muscular pain (Kucera et al., 2005; D'Anchise et al., 2007; Smith & Jacobson, 2011; Wurglics & Ude, 2012), and in the case of low back pain (Giannetti et al., 2010; Staiger, 2012; Pabst et al., 2013); b) the antalgic action of SO ointment, both in terms of rest and exercise (Kucera et al., 2004); c) correlation between pain and anxiety (Esteves et al., 2013; Domenech et al., 2013; Thibodeau et al., 2013).

*Differences* compared to SO studies would include the following: a) our study demonstrates the reducing effect on pain sensation under moderate physical exertion conditions of pedaling on a stepper, for sedentary subjects with lumbar pain treated with PSO prior to exercise; b) highlighting the correlation between pain sensation and anxiety; c) finding the effect that the chosen pain therapy with PSO may indirectly have on reducing anxiety, which correlates with physical exertion.

## Conclusions

1. At the end of PSO ointment therapy, both after the first and the second period of phytotherapeutic preparation use, the sensation of pain was significantly reduced in subjects with subacute lumbar pain.

2. The pain sensation and anxiety were significantly reduced in subjects treated with PSO ointment compared with untreated subjects under moderate physical exertion conditions of pedaling on a stepper.

3. PSO ointment phytotherapy provided antalgic and emotional protection in the treated subjects, under moderate exercise conditions by stepper pedaling.

4. Given the results obtained with PSO ointment, as well as its therapeutic qualities of good tolerance by the body, absence of toxicity and economic accessibility, we propose its use by subjects with subacute low back pain, as a form of pain therapy and antalgic protection under rest and moderate exercise conditions.

## Conflicts of interest

Nothing to declare.

## Acknowledgement

We would like to thank Doctor Alexandrina Fărăgău, for kindly hosting this study in the medical practice that she runs, and Eng. Dr. Nicolae Colceriu for botanical counseling and for his contribution to statistical data processing.

The financing of the study was obtained from sponsorships.

## References

- Bogduk N. Pharmacological alternatives for the alleviation of back pain. *Expert Opin Pharmacother*, 2004; 5(10):2091-2098.
- Cameron M, Chrubasik S. Topical herbal therapies for treating osteoarthritis. *Cochrane Database Syst Rev*, 2013; 31:5:CD010538. doi: 10.1002/14651858.CD010538.
- Cronbach, L.J. Coefficient alpha and the internal structure of tests. *Psychometrika*, 1951; 12:297-334.
- Cronbach, L.J. My current thoughts on coefficient alpha and successor procedures. *Educational and Psychological Measurement*, 2004; 64:391-418.
- D'Anchise R, Bulitta M, Giannetti B. Comfrey extract ointment in comparison to diclofenac gel in the treatment of acute unilateral ankle sprains (distortions). *Arzneimittelforschung*, 2007; 57(11):712-716.
- Domenech J, Baños R, Peñalver L, Garcia-Palacios A, Herrero R, Ezzedine A, Martinez-Diaz M, Ballester J, Horta J, Botella C. Design considerations of a randomized clinical trial on a cognitive behavioural intervention using communication and information technologies for managing chronic low back pain. *BMC Musculoskelet Disord*, 2013; 22(14):142.
- Ellegaard H, Pedersen BD. Stress is dominant in patients with depression and chronic low back pain. A qualitative study of psychotherapeutic interventions for patients with non-specific low back pain of 3-12 months' duration. *BMC Musculoskelet Disord*, 2012; 6(13):166.
- Esteves JE, Wheatley L, Mayall C, Abbey H. Emotional processing and its relationship to chronic low back pain: Results from a case-control study. *Man Ther*. 2013; pii: S1356-689X(13)00086-6. doi: 10.1016/j.math.2013.05.008. [Epub ahead of print]
- Gagnier JJ, van Tulder M, Berman B, Bombardier C. Herbal medicine for low back pain. *Cochrane Database Syst Rev*, 2006; 19(2):CD004504
- Giannetti BM, Staiger C, Bulitta M, Predel HG. Efficacy and safety of comfrey root extract ointment in the treatment of acute upper or lower back pain: results of a double-blind, randomised, placebo controlled, multicentre trial. *Br J Sports Med*, 2010; 44(9):637-641.
- Ivo R, Nicklas A, Dargel J, Sobottke R, Delank KS, Eysel P, Weber B. Brain structural and psychometric alterations in chronic low back pain. *Eur Spine J*, 2013 Feb 8. [Epub ahead of print]
- Jurcău R, Jurcău I, Bodescu C. Anxiety and salivary cortisol modulation, in stress sports, by the help of a phytotherapeutic produce that contains *Rhodiola Rosea*. *Palestrica Mileniului III*, 2012a; 13(3):213-218.
- Jurcău R, Jurcău I, Bodescu C. Emotional and oxidative changes in stress produced by short term and heavy physical effort. *Palestrica of the Third Millennium*, 2011; 12(4):349-354.
- Jurcău R, Jurcău I, Bodescu C. Heart rate and salivary cortisol changes in short term and heavy stress sports, to the untrained people. *Palestrica Mileniului III*, 2012b;13(2):101-105.

- Jurcău R, Jurcău I. Influence of music therapy on anxiety and salivary cortisol, in stress induced by short term and heavy sport. *Palestrica Mileniului III*, 2012; 13(3):321-325.
- Jurcău R. The relationship between sports and polyphenols, retrospective analysis of PubMed publications of the last 52 years. *Palestrica Mileniului III*, 2012; 13(3):339-347.
- Kucera M, Barna M, Horáček O, Kálal J, Kucera A, Hladikova M. Topical symphytum herb concentrate cream against myalgia: a randomized controlled double-blind clinical study. *Adv Ther*, 2005; 22(6):681-692.
- Kucera M, Barna M, Horáček O, Kováriková J, Kucera A. Efficacy and safety of topically applied Symphytum herb extract cream in the treatment of ankle distortion: results of a randomized controlled clinical double blind study. *Wien Med Wochenschr*, 2004; 154(21-22):498-507.
- Loeser JD, Treede RD. The Kyoto protocol of IASP Basic Pain Terminology. *Pain*, 2008; 137(3):473-477.
- Pabst H, Schaefer A, Staiger C, Junker-Samek M, Predel HG. Combination of comfrey root extract plus methyl nicotinate in patients with conditions of acute upper or low back pain: a multicentre randomised controlled trial. *Phytother Res*, 2013; 27(6):811-817.
- Reips UD, Funke F. Interval-level measurement with visual analogue scales in Internet-based research: VAS Generator. *Behavior Research Methods*, 2008; 40(3):699-704.
- Reisner L. Biologic poisons for pain. *Curr Pain Headache Rep*, 2004; 8(6):427-434.
- Scott J, Huskisson EC. Graphic representation of pain. *Pain*, 1976; 2:175-184.
- Smith DB, Jacobson BH. Effect of a blend of comfrey root extract (*Symphytum officinale* L.) and tannic acid creams in the treatment of osteoarthritis of the knee: randomized, placebo-controlled, double-blind, multiclinical trials. *J Chiropr Med*, 2011; 10(3):147-156.
- Spielberger CD, Gorsuch RL, Lushene PR, Vagg PR, Jacobs AG. *Manual for the State-Trait Anxiety Inventory (Form Y)*. Consulting Psychologists Press. Inc. Palo Alto, 1983: 235.
- Staiger C. Comfrey root: from tradition to modern clinical trials. *Wien Med Wochenschr*, 2013; 163(3-4):58-64.
- Staiger C. Comfrey: a clinical overview. *Phytother Res*, 2012; 26(10):1441-1448.
- Thibodeau MA, Fetzner MG, Carleton RN, Kachur SS, Asmundson GJ. Fear of injury predicts self-reported and behavioral impairment in patients with chronic low back pain. *J Pain*, 2013; 14(2):172-181.
- Wurglics M, Ude C. *Rationale Phytopharmakotherapie bei Schmerzen*. Teufelskralle, Arnika, Beinwell. PZ Prisma, 2012; 19:33-41.

#### Websites

- (1) [http://www.energy.sk/info/menu\\_x2056x.asp](http://www.energy.sk/info/menu_x2056x.asp) - Accessed on 12.04.2013
- (2) <http://www2.energy.sk/info/vyrobky/Zoznam2.asp?druh=4> - Accessed on 12.04.2013
- (3) <http://www.medicalexpo.com/prod/runner/steppers-69883-433233.html> - Accessed on 12.04.2013