reports of the histological changes in lichen sclerosus during pimecrolimus or tacrolimus treatment. There is a small lifetime risk (3-5%) in anogenital lichen sclerosus for the development of squamous cell carcinoma and recently, there has been concerns about the development of cancers and lymphomas in patients using these preparations.
Methods: 29 outpatients with histologically confirmed, active LS were recruited to this study with two aims. First we evaluated the effectiveness of pimecrolimus treatment to LS. Secondly, we evaluated the histological changes during pimecrolimus treatment.
Results: All 29 patients completed the follow-up period. 69% (20/29) were in complete remission including relief from itch, pain and inflammation. There were no systemic adverse reactions. In vulvar differentiated intraepithelial neoplasia (d-VIN), which is a postulated precursor lesion for LS-associated vulvar squamous cell carcinoma (SCC), the atypical keratinocyte p53 expression in a typical finding. Surprisingly, the expression of p53 was down-regulated during pimecrolimus treatment.
Conclusions: In our opinion, patient-applied 1% pimecrolimus cream is safe and effective for the treatment of LS. The decrease of p53 staining during pimecromus treatment is best explained for the decrease of ischaemic stress response due to poor oxygenation, vasculitis and inflammation during healing process.
Keywords: Lichen sclerosus, pimecrolimus, immunomodulation, p53, hypoxic stress response.

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EVALUATION OF THE ESTROGENIC EFFECT OF *NIGELLA SATIVA* USING THE RAT MODELS OF UTEROTROPHIC ASSAY

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Introduction: nigella sativa (Black Seed) have been used as a traditional medicine for the treatment of a variety of sicknesses as well as health status including increase of milk flow and regulation of menstruation in the female.
Objectives: Evaluation of estrogenic activity of *Nigella sativa* using menopause induced rat models.
Methods: *Nigella sativa* was administerd orally as a suplement to chow pellet at different doses of 300, 600 and 1200 mg/kg for 21 days to ovariectomized (OVX) rats and were compared to either Conjugated Equine Estrogen- CEE (0.2mg/kg) as positive or distilled water (1ml) as negative control.
Results: Treatment with *Nigella sativa* resulted to a significant increase in uterine weight as compared to control OVX with altering the serum estrogen levels. Histopathological evaluation of the uterine revealed changes characterized by atrophy of the uterus in OVX controls, while the OVX rats treated with either *Nigella sativa* or CEE showed increased endometrial responses as indicated by proliferation of the endometrial glands, epithelial hyperplasia, dilatation of the lumen as well as increased number of glands and vascularity. Surprisingly, the low dose of *Nigella sativa* revealed higher estrogenic effects than other dosages.
Conclusions: The observed estrogenic effect following *Nigella sativa* treatment sugests that this amazing herb could possibly act on the estrogen receptors with enhauncing the endogenouse estrogen levels. *Nigella sativa* showed the desired effects on rats' reproductive performance, thereby indicating its beneficial rols in the treatment of the postmenopausal symptoms.
Keywords: *Nigella sativa*, Estrogenic Effects, Uterotrophic Assay, Ovariectomized Rats

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EFFECTIVENESS OF TWO REGIMES OF GLUCOSAMINE AND CHONDROITIN FOR TREATMENT OF PAIN SYNDROME IN PATIENT WITH KNEE OSTEOARTHRITIS

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Objectives: The research was aimed at evaluating the effectiveness of two regimes (continuous and interrupted) of Theraflex (500 mg glucosamine hydrochloride, 400 mg chondroitin sulphate) in patients with knee osteoarthritis. Outcomes evaluated were pain, measures of performance (function, activity of daily living, disability), employment status, range of motion, and patient satisfaction/patient global perceived effects.
Methods: The first group included 50 patients (aged 64.5±1.1 years) with knee osteoarthritis (II stage, Kellgren-Lawrence's classification), who took the drug in continuous regime during 9 months. The second group included 50 patients with the same diagnosis (aged 64.6±1.0 years), who took Theraflex twice during 3 months with 3 months interruption. We examined the patients before the treatment and after 1, 3, 6, 9 and 12 months. Methods of study: Mc-Gill questionnaire, visual-analogical scale (VAS), Lequen's index, WOMAC, EuroQol-5D, 15-m. test, 6-min. test.
Results: After three months of Theraflex's treatment it was observed a reliable decrease of pain syndrome in both groups by WOMAC, decrease of constraint in movements, improvement of index of everyday activity, VAS, 15-m.test. Examination of patients during 6,9 and 12 months show the effectiveness of both regimes of the therapy. Intensity of pain syndrome and functional activity didn't differ between the groups.
Conclusions: During 1-year period two regimes of Theraflex it was established effective decrease of intensity of the pain syndrome and improvement of everyday activity in patients with knee osteoarthritis. The analgesic effect after taking Theraflex becomes noticeable after three months and quality of life significantly improved in patients of both groups.
Keywords: Glucosamine, chondroitin, osteoarthritis.

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OPEN PLACEBO-CONTROLLED STUDY OF THE EFFICACY OF PHENIBUT IN TREATING CHRONIC NECK PAIN AND MENOPAUSAL SYMPTOMS IN POSTMENOPAUSAL WOMEN

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Objectives: The aim was to study the efficiency of phenibutum (Noophen®) in complex treatment of chronic neck pain and menopausal symptoms in the women in early postmenopausal period.
Methods: It was examined 30 postmenopausal women with chronic neck pain, which took Noophen on 1 tablet (250 mg) 2 times per day during 30 days (I group). Second (II) group (n=20) accepted Noophen-placebo on the same circuit. Both groups were similar as regards age, duration of menopause and age at menopause ($p>0.05$).We used X-ray method, questionnaires and studied the evaluation of pronouncement of the pain syndrome, psycho-emotional displacements, distinctness of climacteric syndrome, definition of jet and individual alarm, state of vegetative nervous system, biological age.The inspections were carried out in the beginning of treatment, on 15 and 30 days from a beginning of treatment.
Results: It was shown the reduction the intensity of the headache and decreases the neck pain (before treatment - (3,4±0,8), after treatment - (2,0±0,6), $p<0.05$) and menopausal symptoms (Modified Êupperman index: (26,9±1,0) and (17,6±1,2), $p<0.01$), parameters of jet uneasiness (Jet alarm: (35,2±2,0) and (29,8±2,3), $p<0.01$. Individual alarm: (59,4±2,1) and (53,5±0,8), $p<0.05$) in Noophen group. In placebo group of significant changes not got, but only the tendency to reduction of jet ((34,2±1,6) and (32,5±1,2)) and individual ((55,1±1,8) and (51,6±0,8)) alarm, intensity of pain syndrome ((3,9±0,6) and (3,6±0,5)) and climacteric symptoms (Modified Êupperman index (24,7±1,6) and (20,9±0,9)).
Conclusions: Phenibut is effective in the complex treatment of chronic neck pain in early postmenopausal women.
Keywords: Phenibut, menopause, women.