of cinnamon and Ibuprofen for treatment of primary dysmenorrhoea in a sample of Iranian female college students.

The trial was randomised, double-blind and placebo-controlled, with subjects allocated to receive Ibuprofen capsule containing 400mg three times daily (TDS), *Cinnamomum zeylanicum* capsule containing 420mg cinnamon as dried powder TDS, or a placebo capsule containing starch TDS, for 24 hours. In total, 114 female college students were recruited for the trial, with 38 subjects in each study arm. Inclusion criteria included: being aged 18-30 years; regular menstrual cycles; moderate dysmenorrhea;, lack of chronic diseases; not having symptoms such as burning, itching or abnormal vaginal discharge; lack of pelvic inflammatory disease, tumour, or fibroma; lack of recent stressors; and within defined body mass index range of 19-26 kg/m^2. Exclusion factors included: oral contraceptive pill use; medicine or plant allergy; and mild dysmenorrhea. Pain intensity and duration of pain were monitored for subjects in the first 72 hours of cycle. To determine the severity of pain a Visual Analogue Scale (VAS) was employed, and the Cox Menstrual Scale was used to determine the duration of pain.

Baseline characteristics between groups were similar, with similar pain scores reported before treatment. After treatment, the mean pain severity score reported for Ibuprofen was significantly less that the placebo group from the first time interval of 1hr post treatment, and at each subsequent interval til 72hrs. For the cinnamon group, no statistically significant difference in pain severity score was observed for the first four hours compared to placebo. After the next time interval of 8hr post intervention, however, a statistically significant reduction in pain severity was observed in the cinnamon group compared to placebo that continued til the end of observation at 72hrs. Duration of pain in the Ibuprofen and cinnamon groups were reported to be significantly less than placebo at reported time intervals after intervention. The effect of cinnamon was lower than that observed with Ibuprofen.

The study and the interpretation of its findings are limited by a lack of clarity around the plant and timing of interventions. The authors do not report on the part of plant used nor describe the preparation of plant material. Furthermore, it is unclear from the study when the intervention was initiated, i.e. at onset of menstruation, at onset of pain or another set time point, whether the intervention timing was standardised amongst study subjects, and whether the results were time after the initial or final dose of the intervention. Some discrepancy in tables provided also limit interpretation of the data.

The study provides some evidence for the use of *Cinnamomum zeylanicum* in dysmenorrhoea, demonstrating that compared to placebo, cinnamon intervention significantly reduced the severity and duration of pain during menstruation, albeit to a lesser extent that Ibuprofen. For women looking for non-pharmaceutical management of dysmenorrhoea, cinnamon may provide some benefit. Whilst the study seems to be a reasonably well-designed trial, it is unfortunate that presentation of data and unclear definitions of the therapy limit the interpretation and ability to apply the findings more broadly. Future studies that address some of these limitations, and with greater numbers of subjects, will further understanding.

Berberis integerrima compared to sildenafil in pulmonary hypertension

Mahdavi N, Joukar S, Najafipour H, Asadi-Shekaari M. 2015. The promising effect of barberry (Zereshk) extract against experimental pulmonary microvascular remodelling and hypertension: A comparison with sildenafil. *Pharm Biol*. In press. DOI: 10.3109/13880209.2015.1050676.

Pulmonary arterial hypertension (PAH) is described as a mean pulmonary artery pressure ≥ 25 mmHg at rest or ≥ 30 mmHg with exercise and a normal pulmonary capillary wedge pressure. PAH may be primary or idiopathic, or associated with other diseases including HIV infection, connective tissue disease, portal hypertension, and congenital heart disease. Untreated, the survival time for idiopathic PAH has been reported to be three years, with the prognosis of secondary PAH influenced by the underlying disease. Three main classes of drugs are currently used for treatment of PAH including prostanoids, enothelin-1 receptor antagonists, and phophodiesterase-type 5 (PDE5) inhibitors. While these medications can attenuate clinical symptoms and slow PAH development, they are not cures for the disease and accordingly interest remains for potential new therapies.

The major chemical constituents of the fruits of *Berberis integerrima* (barberry), of the Berberidaceae family, include coumarin, ascorbic acid, berberine, caffeic acid, β-carotene, flavonoids, malic acid, palmatine, carbohydrates, tannin, and ursolic acid. Whilst related to another barberry species, *Berberis vulgaris*, comparisons between the two species report differences in chemical make-up such as higher total phenolic and anthocyanin content in the fresh fruits of *B. integerrima*. Traditionally used for treatment of heart conditions including hypertension and arrhythmia, pharmacological studies on barberry and its key constituent berberine have demonstrated effect on decreasing systemic hypertension. Following from this, authors conducted the present study to examine the effect of a water extract of barberry (*B. intergerrima*) fruit on a monocrotaline-induced PAH rat model and compare its effect with sildenafil, a PDE5 inhibitor.

Seventy-two male Wistar rats were divided into nine groups as follows: the control group, the monocrotaline (M) group, the barberry (B) groups with doses of 50, 100,

and 200 (mg/kg/d), the M plus barberry (MB) groups with doses of 50, 100, and 200 (mg/kg/d) barberry, and the M plus sildenafil group (30mg/kg/d). Two weeks after a single injection of monocrotaline (60 mg/kg) to induce PAH on day one of the study, barberry water extract or sildenafil were gavaged daily for two weeks. At the end of the 4th week, hemodynamic, biochemical, and histopathological parameters were assessed.

After two weeks of intervention, both sildenafil and barberry at all doses significantly reduced the right ventricular systolic pressure (RSVP) compared with the M group. The effect on RSVP reduction was comparable between barberry MB100 and MB200 mg/kg and the sildenafil group. Right ventricular hypertrophy was significantly reduced in the sildenafil group and the MB100 and MB200 compared to the monocrotaline group. Histopathological parameters were only evaluated in the MB200 group, which had previously demonstrated the greatest effect in the hemodynamic parameters. Both sildenafil and MB200 intervention attenuated the monocrotaline-induced arteriole remodelling resulting in significant reduction in the medial wall thickness. The effect was significantly greater in the barberry intervention compared to sildenafil. Neither barberry nor sildenafil had any significant effect on the plasma levels of endothelin-1, glutathione peroxidase, and the malondialdehide of lung.

This interesting study demonstrated a beneficial effect of a barberry water extract on a monocrotaline-induced rat model of pulmonary hypertension. Furthermore, when compared to sildenafil, a currently used therapy for PAH, barberry demonstrated equivalent or greater effect at a dose of 200mg/kg/d. Authors suggest that the effect of barberry may be attributable to a combination of its phenolic and alkaloid compounds, potentially with some effect on redox balance. The study provides some good preliminary research and evidence for further exploring the potential of barberry or its derivatives in the treatment and management of pulmonary arterial hypertension.

Effectiveness of ginger for relieving symptoms of primary dysmenorrhea

Daily JW, Zhang X, Kim DS, Park S. 2015. Efficacy of ginger for alleviating the symptoms of primary dysmenorrhea: A systematic review and meta-analysis of randomised clinical trials. *Pain Med*. In press. DOI: 10.1111/pme.12853.

Primary dysmenorrhea is one of the most common gynecologic disorders, with a prevalence (of varying severity) of between 30-90% amongst different ethnicities with. Severe dysmenorrhea is estimated to contribute to a loss of 600 million work hours and $2 billion in lost productivity per year. Whist the cause of primary dysmenorrhea is not fully understood, it is known that increased production of prostaglandins derived from inflammatory mediators, including cyclooxygenase (COX)-2, cause excessive contractions of the uterus with associated pain and cramping. Non-steroidal anti-inflammatory drugs (NSAIDs), which inhibit COX-2, are the main treatment for primary dysmenorrhea, butthey are not completely effective and have considerable adverse effects, morbidity and mortality associated with their use. Accordingly, there is interest in interventions that provide efficacy and are well tolerated.

The root of *Zingiber officinale* (ginger) has previously demonstrated anti-inflammatory activity through inhibition of COX-2, NF-κB and 5-lipoxygenase (5-LOX). Additionally, ginger may act as an agonist of transient receptor potential cation channel subfamily V member 1 (TRPV-1), which is associated with transmission of physical and chemical stimuli, and is a target for novel pain relievers in development. With growing evidence that ginger has analgesic and anti-inflammatory efficacy in humans, the current study is the first systematic review and meta-analysis of randomised clinical trials (RCTs) assessing the effectiveness of ginger for primary dysmenorrhea.

In the undertaking of the systematic review, electronic databases including PubMed, EMBASE, Cochrane Library, Korean databases, Chinese medical databases and Indian medical journals were searched with key terms "ginger", "*Zingiber officinale*", "dysmenorrhea", and "pain". Randomised clinical trials that studied the effect of ginger on primary dysmenorrhea as a primary outcome in young women were included. Exclusion criteria included in vitro studies, studies where only an abstract was available, nonclinical trials, studies in which ginger formed part of a complex herbal mixture, and duplicate studies.

Of 29 publications initially identified, seven articles were included in the review. All of the RCTs investigated the effect of ginger powder, at varying doses between 750-2000mg/day during the first 3-4 days of menstrual cycle, with each study lasting for two cycles. The age of women enrolled ranged from 13-30 years. Of the RCTs, four compared ginger powder to placebo, one RCT compared ginger powder + exercise to exercise alone, and the remaining two RCTs compared ginger to active analgesic treatments. Outcome measures in the meta-analysis included severity of pain during menstruation, using a pain visual analogue scale (PVAS) and the duration of pain. Of the RCTs in the review, five used PVAS scores, whilst two reported scores as a percentage change from baseline. Of the five using real scores, one did not include standard deviations and one used exercise as its control, leaving only three RCTs, comparing ginger to placebo control, included in the meta-analysis.

When pooling the data of the three RCTs, the meta-analysis indicated that ginger is highly effective for the treatment of symptoms of primary dysmenorrhea, with significantly lower pain scores in the ginger group compared to the control across both one and two cycles. The relief from pain was also highly significant in studies