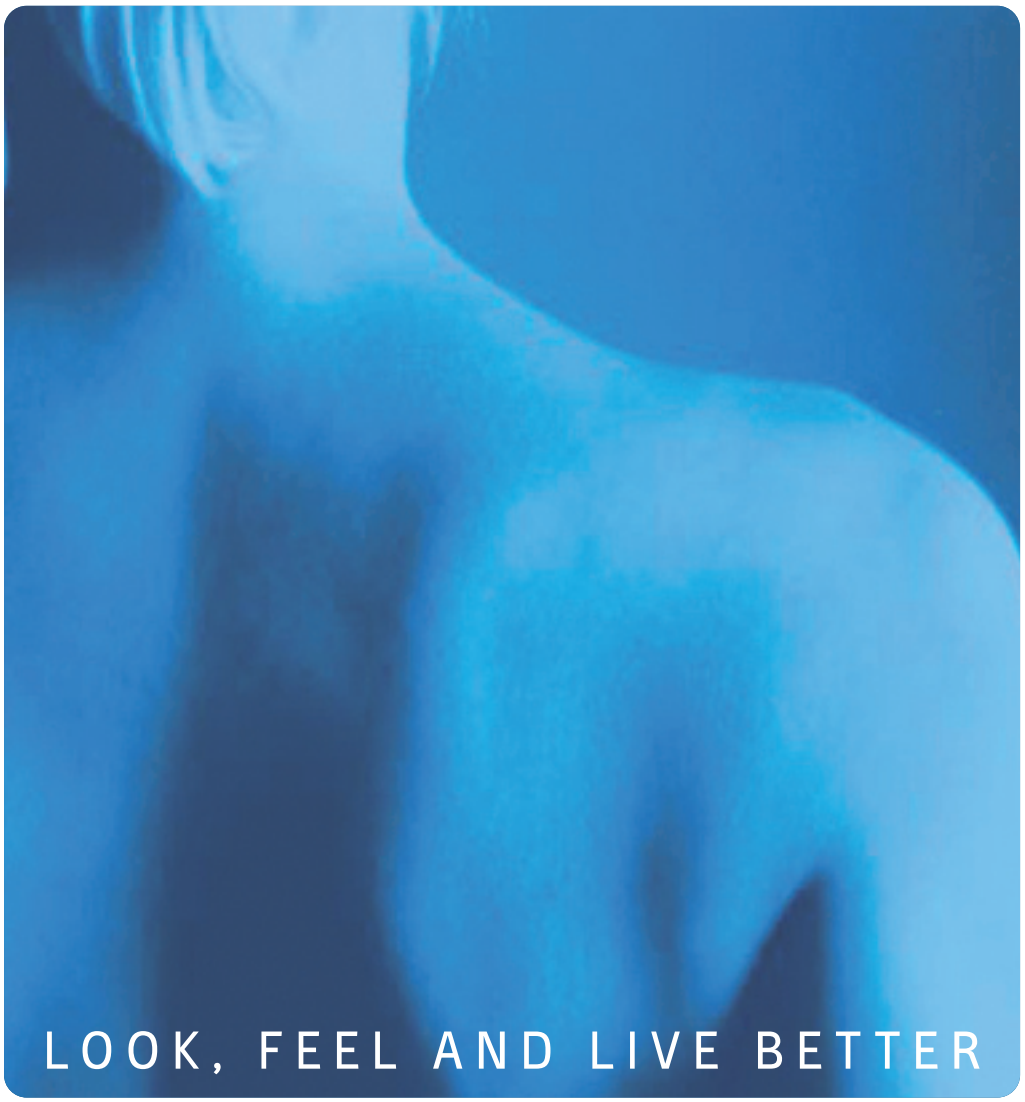
PYCNOGENOL

Menstrual Discomfort



HORPHAG

Pycnogenol® for Menstrual Discomfort

Most women of child-bearing age experience a variety of symptoms related to the menstrual cycle that may be limited to milder discomfort such as from the pre-menstrual syndrome or extend to serious menstrual pain which seriously affects quality of life. The complete replacement of tissue lining the uterine cavity, the endometrium, during the menstrual period represents a wound healing process and involves inflammatory processes.

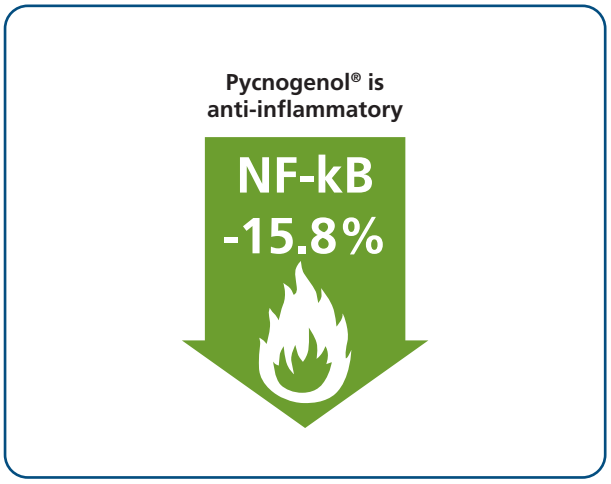
The inflammation is initiated by prostaglandins developing during menstruation which causes uterine contractions and pain. Some women experience menstrual pain levels which severely interfere with daily functions and affects quality of life. In medical terminology this is known as dysmenorrhoea.

The prevalence of dysmenorrhoea is highest in adolescent women, with estimates ranging from 20% to 90% depending on the diagnosis standards applied [French, 2005]. For women dysmenorrhoea is the most common reason for absence from work.

Pycnogenol® inhibits prostaglandins and is anti-inflammatory

The standard regimen for dysmenorrhoea are "over the counter" non-steriodal antiinflammatory drugs (NSAID) such as ibuprofen. These medications reduce menstrual pain efficiently and quite rapidly. However, these pain-killers have side effects causing gastric problems and other more serious complications, particularly when they are taken in high quantities as it is typical in dysmenorrhoea. A clinical study has shown that consumption of Pycnogenol® non-selectively inhibits COXenzymes, which are involved in synthesis of pro-inflammatory prostaglandins during the menstrual period. Already after a single dose of Pycnogenol® both COX-1 and COX-2 enzymes are significantly inhibited in humans by 22.5% and 14.7%, respectively [Schäfer et al., 2006].

Furthermore, Pycnogenol® was shown to lower the inflammatory master switch (NF-kB) in humans after five days of continuous consumption by 15.8% [Grimm et al., 2006]. NF-kB triggers the generation of essentially all pro-inflammatory mediators. This provides the basis for the rationale to use Pycnogenol® to naturally moderate inflammatory processes and pain sensation involved in menstruation. Additionally, Pycnogenol® supports the wound healing process and stabilises capillaries which will help to speed-up the recovery of the endometrium.



Japanese gynaecologists discovered Pycnogenol® soothes menstrual pain

Two Japanese gynaecologists tested Pycnogenol® for lowering menstrual pain in an open, uncontrolled exploratory trial. Thirty nine women with dysmenorrhoea or endometriosis were treated with 30 mg Pyc-

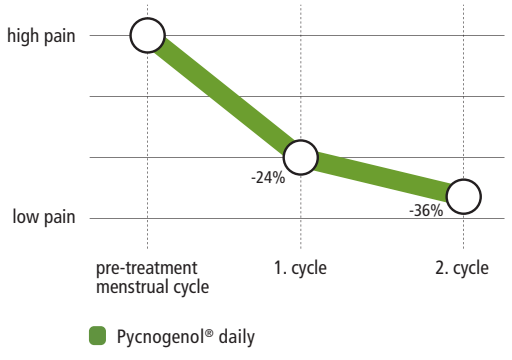
nogenol® daily starting seven days before menstruation. Both abdominal pain and cramping were found to be improved in the majority of women [Kohama & Suzuki, 1999]. These initial findings have prompted further research of benefits of Pycnogenol® for menstrual discomfort.

Pycnogenol® relieves menstrual pain

A clinical trial in Japan investigated 47 women who were diagnosed having symptoms of dysmenorrhoea. Their pain sensation and use of pain medication was recorded throughout the trial, which covered three complete menstrual cycles. The first, pre-treatment menstrual cycle served for establishing baseline pain level and analgesic use. Directly after completion of the pre-treatment cycle women took Pycnogenol® every day until completion of two further menstrual cycles.

The results showed that women had significantly less abdominal pain when they had started taking Pycnogenol® three weeks before their period. The pain relief was even more pronounced during the following period, with the pain score reduced by 36% compared to pre-treatment. The number of days during which women experienced menstrual pain was likewise lowered from average pre-treatment 3.9 days to 3.6 and 3.3 days in the first and second period, respectively. Women required less pain medication during their menstrual period when they took Pycnogenol®.

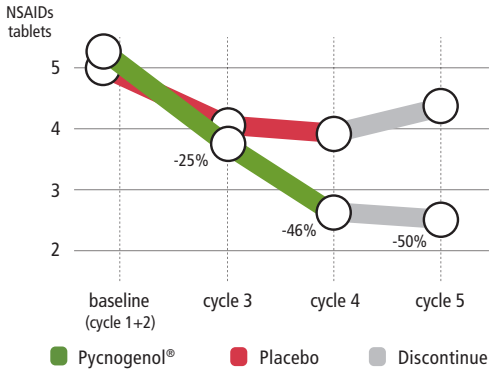
Pycnogenol® gradually decreases menstrual pain



Multi-centre field study with Pycnogenol® for menstrual pain

Four hospitals in Japan investigated a total number of 116 women suffering from menstrual pain in a multi-centre, randomised, double-blind, placebo-controlled fashion [Suzuki et al., 2007]. The first two pre-treatment menstrual cycles were utilised for establishing base-line values for pain sensation and analgesic medication use. During the following 2 menstrual cycles women were randomly assigned to groups receiving daily regimens of Pycnogenol® or placebo. Thereafter, regimen was discontinued to investigate the recurrence of symptoms.

Women required less pain medication during menstruation



Treatment with Pycnogenol® lowered pain during menstruation, which was reflected by a significant reduction of pain medication used. The number of painful days due to dysmenorrhoea was decreased from average 2.1 days prior to treatment to 1.3, 1.3 and 1.2 days during the consecutive menstrual cycles, respectively. Discontinuation does not cause an immediate relapse as pain levels and pain medication use did not increase. As in previous studies on dysmenorrhoea the pain relief develops gradually during supplementation with Pycnogenol®.

Endometriosis

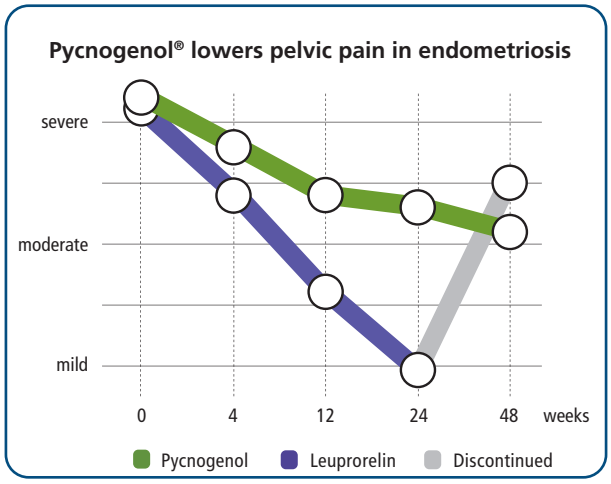
Endometriosis is a condition involving the tissue that covers the uterine cavity (endometrium), which is shed during menstruation. In endometriosis this tissue has movedoutside the uterus and grown elsewhere in the body. The most common places withdisplaced endometrium are the ovaries, the oviducts, the uterine wall, lining of the pelvis andeven the bladder and intestines. How the endometrial cells reach other organs remainsunknown. The displaced tissue behaves like uterine endometrium in responding to themonthly cycle. Bleeding occurs but cells cannot exit the body, and painful inflammationerupts. In every cycle the growths adds extra tissue and for this reason endometriosissymptoms tend to get worse over time.

Standard treatment involves NSAIDs for pain relief. In more advanced cases surgery isconsidered the best treatment option. Hormonal treatment is commonly applied fortreatment of endometriosis. Oral contraceptives block the effects of natural hormones onendometrial growth, which can make endometriosis less painful. The most effectivetreatment is achieved with the synthetic peptide Leuprorelin which blocks oestrogenproduction. Leuprorelin cannot be taken orally and therefore and a long-lasting depot isinjected under the skin. The disadvantage of Leuprorelin is the interruption of menses andwomen cannot get pregnant. The treatment is limited to 6 months because of the risk forosteoporosis and after discontinuation a relapse is very likely.

Pycnogenol® is helpful for women with endometriosis

The possibility of improving endometriosis with Pycnogenol® was investigated in acomparative clinical study with 58 women receiving either Pycnogenol® or Leuprorelin [Kohama et al., 007]. All women had undergone surgical treatment of endometriosis within 6months prior to participation. They suffered recurrent moderate to severe endometriosis andrefused further surgery.

Treatment with Pycnogenol® graduallydecreased menstrual pain from initial severepain to moderate pain at trial end. The painscore was lowered significantly by 33% during the treatment period. Leuprorelinsuppressed menstruation during treatment.Pycnogenol¨ was effective for slowly butsteadily decreasing pelvic pain from initialsevere to moderate pain. Leuprorelin wassignificantly more effective; however, adramatic relapse occurred within 24 weeksafter obligate discontinuation.



A specific antigen (CA-125) is shed from inflamed endometriomas into the blood stream andserum CA-125 is considered a good marker for evaluation of the severity of advancedendometriosis. Pycnogenol® significantly lowered serum CA-125 indicating a reduction ofendometrioma size. Lowering of CA-125 was dramatically more effective with Leuprorelin,however, values almost returned to baseline after discontinuation.

As expected Leuprorelin drastically lowered women's oestrogen level. In contrast, over thewhole treatment period Pycnogenol® did not influence women's oestrogen level.

In conclusion, Pycnogenol® is significantly effective for improving endometriosis, though it isnot as effective as oestrogen-inhibition with Leuprorelin. The advantage of Pycnogenol® isthe absence of severe side effects. Interestingly, five women with endometriosis taking Pycnogenol® left the study because they became pregnant.

The application of Pycnogenol® for dysmenorrhoea and endometriosis is patented (US patent6,372,266.).

Clinical research suggests Pycnogenol® provides significant benefits for women living with menstrual discomfort:

- Soothing of pain during the menstrual period
- Natural anti-inflammatory activity
- Less pain medication is required
- Less days with menstrual pain
- Improvement of endometriosis
- Oestrogen levels remain unaffected

References

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