

# Melatonin

**Melatonin** is the natural hormone produced in the pineal gland in the brain. It acts as an internal body clock, to regulate circadian/ biological rhythms.

**Pinealectomy** (removal of the gland) enhances tumour growth and metastasis in experimental animals. Pineal extracts, even if melatonin-free, inhibit human cancer cells.

**Working rotating night shifts or going to bed after 2AM** increases risk of breast cancer, presumably due to suppression of melatonin production. Normally melatonin levels peak between 2 and 3AM. Melatonin suppresses the synthesis and secretion of sex hormones.

**Melatonin production** is suppressed by morning light, and that promotes alertness. Beta-blocker drugs prescribed for high blood pressure and fast heart beat will also depress melatonin secretion.

**Long-term safety** as a supplement is well established. For insomnia and jet-lag use 1 to 3 mg at bedtime. The type of sleep issue it tends to help is when people are trying to sleep at a time other than the usual 10PM to 6AM. It can treat **gastro-esophageal reflux disorder GERD**. For cancer we target 10 to 60mg, to tolerance at "bedtime" only!

**IMPORTANT NOTE:** Never take melatonin at any other time than at bedtime - what we call "the hour of sleep" - in the late evening. This is 8PM to 12 midnight only! If you forget to take it during the prescribed time of day, wait until the next evening. The dose is reduced if you have nightmares or feel groggy in the morning. After about 3 years of use the dose should drop to a maximum of 5 to 6 mg at bedtime.

**Avoid melatonin** for disseminated cancers such as leukaemia, lymphoma and multiple myeloma. It may be used in such cases only short-term during chemo or radiation, if prescribed by a physician experienced in integrative oncology.



# Melatonin Continued

Melatonin is a balancer and stabilizer in all stages of solid tumours, melatonin is also very helpful in most cancers, not just hormone dependent types.

- Improves survival time as a sole agent in terminal cancer
- Doubles survival time and response rate to conventional therapy in all hormone sensitive cancers
- Antioxidant in low doses, protecting DNA, RNA and cellular membranes from oxidation
- Pro-oxidant in cancer cells at higher doses
- Inhibits cancer initiation, anti-carcinogenic
- Modulates hormones - estrogen, testosterone, prolactin and may make tumours more hormone dependent, which is more amenable to treatment
- Blocks mitogenic effects of hormones and growth factors
- Melatonin directly and indirectly inhibits epidermal growth factor receptor EGFR
- Increases effectiveness of radiotherapy, reduces myelodysplasia
- Increases gap junctional intercellular communication
- Controls fatty acid uptake, transport and metabolism, by suppression of cAMP at plasma membranes
- Improves glucose tolerance
- Increases p53 expression
- Increases apoptosis
- Modifies cytokines, increasing host immune defences via thymus and T-helper cell derived opioid peptides, and enhances thymocyte proliferation
- Immuno-modulator - increases INF $\gamma$ , IL 1, 2, and 12
- modulates cortisol stress hormone, reducing its suppression of immune function• decreases circulating cytokine interleukin 6 (IL-6) significantly
- Synergetic with IL-2 therapy, increases effectiveness up to ten fold, allowing use of only 10% of the usual dose
- NK cells have receptors for melatonin and IL-2; melatonin increases NK number and lytic activity
- Inhibits NF $\kappa$ B transcription factor, reducing pro-inflammatory cytokines
- Inhibits AP-1 activator protein, decreasing cancer cell proliferation
- Down-regulates 5-lipoxygenase gene expression
- Reduces TNF secretion
- Reduces cachexia, along with omega 3 EPA and antioxidants R+ alpha lipid acid, grapeseed extract OPCs, and vitamins C and E



# Melatonin Continued

- Increases response and survival with chemotherapy - reduces myelosuppression (bone marrow damage) and thrombocytopenia (loss of platelets needed for blood clotting)
- Melatonin levels tend to be lowest in estrogen - receptor positive breast cancer cases
- Aromatase inhibitor/ down-regulator, blocking estrogen bio-synthesis from testosterone via CYP-19 aromatase and NADPH-CYP reductase, at serum levels of 1 nM - as seen with natural nighttime synthesis of melatonin in healthy subjects
- Decreases production of estrogen receptors in breast cells, and is a primary selective ER modulator, and therefore synergistic with Tamoxifen
- Increases serotonin, which has an anti-depressant effect
- Naturally increases with meditation (focused awareness exercises) or breathing exercises
- Naturally increases with aerobic exercise
- Occurs naturally in rice, corn and oats
- Inhibits telomerase
- Increases p53
- Thermo-regulator

Melatonin levels and cycles can be naturally regulated by sleeping in a completely dark room between 10PM and 6AM, for a period of at least one month. A night-mask may be used.

Melatonin production is said to be disrupted by electro-magnetic fields, so it is recommended that no electrical appliances or outlets be within 1 meter from your head during sleep. If possible get at least 20 minute exposure to outdoor natural light in the early morning hours.

