



# Endorphins-A Forgotten Hidden Magic Holistic Healer: Mini Review



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## Abstract

**Aim:** Endorphins are endogenous morphine, neuropeptide, produced from pituitary gland in response to stress and pain. There are three types of endorphins are beta-endorphins, dynorphins, enkephalins binds to mu, kappa, delta receptors found on immune cells and nervous system. Beta-endorphins is a most abundant endorphins synthesized and stored in the anterior pituitary gland.

**Material and methods:** To search and find out about endorphins and their mechanism of action in treatment of diseases such as cancer, autoimmune diseases and infectious diseases.

**Results:** It has got various activities such as immune stimulatory, anti-inflammatory, analgesic activity, delay aging, stress buster activity involved in preventive, promotive, therapeutic and palliative treatment of various diseases such as cancer; auto-immune diseases, infectious diseases.

**Conclusion:** Endorphins especially beta- endorphins involved in preventive, promotive, therapeutic and palliative, holistic treatment of various diseases such as cancer; auto-immune diseases, infectious diseases, without adverse effects and inexpensive.

**Keywords:** Cortisol; HPA-axis; P53; NF-KB; STAT-3; Noradrenaline

**Abbreviations:** IL-1: Interleukin 1; IL-2: Interleukin 2; IL-6: Interleukin 6; IL-12: Interleukin-12; TNF- $\alpha$ : Tumor Necrosis Factor-Alpha; NF-kB: Nuclear Factor-kappa B receptor; STAT-3: Signal Transducer and Activator of Transcription-3; Th1: Type 1 helper cells; Th2: Type 2 helper cells; mmp-2,9: matrix-metallo proteases 2,9; Tregs: Regulatory T cells; IL-18: Interleukin 18; IFN- $\gamma$ : Interferon Gamma; IL-10: Interleukin 10; CRH: Corticotrophic Releasing Hormone; HPA-Axis-Hypothalamo Pituitary Adrenal Axis

## Introduction

Endorphins are endogenous morphine, neuropeptides, synthesized in pituitary gland in response to stress and pain mediated release of CRH (Corticotrophic releasing hormone) from hypothalamus activate the release of neuropeptides such as ACTH (Adreno corticotrophic hormone), cortisol and noradrenaline. These neuropeptides activate inflammatory mediators such as IL-1 $\beta$ , TNF- $\alpha$ , IL-6 and COX-2 inflammatory mediators activate key transcription factors such as NF-kB, STAT-3, involved in tumor progression, chronic inflammation, immune modulation leads to auto immunity [1-3].

## Material and Methods

Endorphins are of three types such as beta- endorphins, enkephalins, dynorphins binds to mu, kappa, and delta receptors respectively. Beta-endorphins are the most abundant, potent endorphins, synthesized and stored in the anterior pituitary gland is a precursor of POMC (Pro-opiomelanocortin). Beta-endorphins is an abundant endorphins produced in response to stress and

pain, release CRH from hypothalamus activates HPA-axis through ANS results in release of ACTH, cortisol, and noradrenaline neuropeptides which activates IL-1, TNF- $\alpha$ , IL-6 pro-inflammatory cytokines and COX-2 inflammatory mediator which inturn, activates NF-KB, STAT-3 transcription factors involved in tumor progression by cell proliferation, angiogenesis, cell survival, invasion and metastasis. Beta-endorphins has got various activities such as immunestimulatory, anti-inflammatory, analgesic activity, delay aging, stress buster activity, involved in preventive, promotive, therapeutic and palliative, holistic treatment of various diseases such as cancer; auto-immune diseases, infectious diseases.

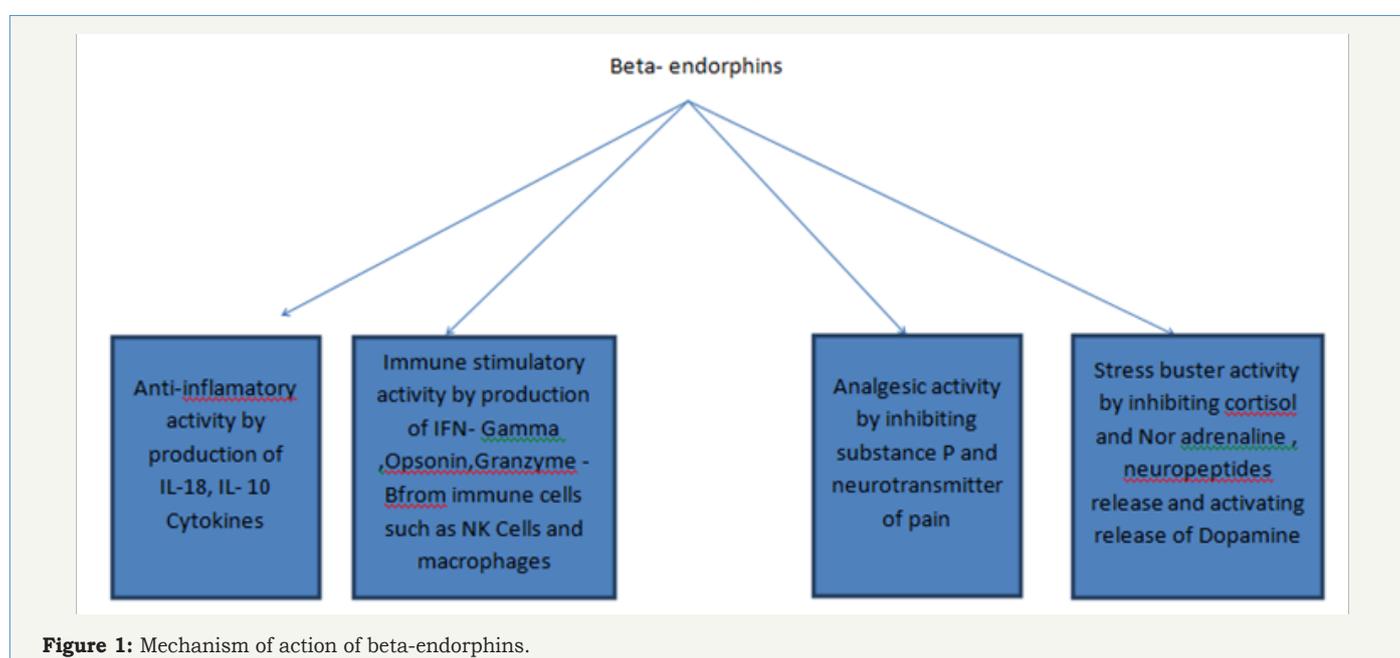
## Discussion

Receptors of endorphins are increased during stressful conditions located on nervous system and immune cells. Receptors of endorphins on peripheral nerves are increased during stressful conditions. Most of all immune cells produce endorphins. In inflammatory condition recruitment of immune cells to the site of inflammation by chemokines produce endorphins, acts as

anti-inflammatory activity by production of anti-inflammatory cytokines such as IL-18, IL-10 and IFN-gamma. Endorphins decrease the activity of sympathetic nervous system, thereby decreasing inflammatory mediators IL-1, TNF- $\alpha$ , IL-6 and COX-2. It inhibits neuropeptides such as cortisol and noradrenaline mediated activation of inflammatory mediators such as IL-1, TNF- $\alpha$ , IL-6, which in turn activates transcription factors NF-KB and STAT-3 involved in tumor progression. Endorphins has an activity of immune stimulatory, endorphins binds on the receptors situated on immune cells such as NK cells, macrophages, T cells and B cells produce IFN-gamma, opsonin, granzyme-B, antibodies, acts as anti-tumor, antiviral, and anti-inflammatory activity [4-8].

In the PNS, binding of endorphins to the receptors on peripheral nerves results in inhibition of substance P, a neurotransmitter of pain and inflammation, results in analgesia and reduce inflammation.

In the CNS, binding of endorphins to the receptors present in CNS results in inhibition of GABA inhibitory neurotransmitter, activation of dopamine neurotransmitter responsible for euphoria, tranquility of mind, stress buster activity and analgesic activity. Beta-endorphins suppress NF-KB, which involves in auto-immune diseases by conversion of TH1 to TH2 lymphocytic type, TH17 cells, alteration in Tregs, which otherwise involved in immune homeostasis and self tolerance, results in immune modulation, cellular changes, tissue damage by matrix metalloproteases, leads to auto-immune disease [9-20] (Figure 1). Beta-endorphins inhibits aging by reducing free radicals release during oxidative burst from inflammatory cells such as tumor associated macrophages, tumor associated neutrophils, dendritic cells and pro-inflammatory cytokines such as IL-1, TNF- $\alpha$ , IL-8 and other mechanism is by lengthening telomeres, which otherwise shortens with aging [21-25].



**Figure 1:** Mechanism of action of beta-endorphins.

Beta-endorphins involved in inhibiting alteration of P53 tumor suppressor gene and its expression in tumor microenvironment by suppressing the antagonistic effect of NF-KB on P53. Suppressing the inflammatory mediators such as free radicals (ROS, RNS) and NO released from tumor associated macrophages, tumor associated neutrophils, DCs involved in mutation of P53 in inflammatory tumor microenvironment and tumor progression. Beta-endorphins increase E-cadherin expression in epithelial cells, which helps in cell adhesion. Loss of E-cadherin involved in epithelial to mesenchymal transition induced tumor invasion [4-10,21-23].

### Factors Responsible for Release of Endorphins

Meditation, pranayama, intense physical exercise, acupuncture, Love, care, music therapy release endorphins. Vigorous physical activity release endorphins creates psychological relaxed state known as runner's high due to release of dopamine

neurotransmitter involved in self reward, euphoria, cognition and addiction. Endorphins are produced in our body in response to stress and pain acts as a holistic preventive, promotive, therapeutic and palliative treatment of choice in autoimmune diseases, cancer, infectious diseases, without adverse effects and inexpensive.

### Comments

- Activities that produce endorphins.
- Quantity of endorphins produces during activities.
- Duration of various effects by endorphins need to be known.
- Mechanism of actions of different types of endorphins.
- Thorough understanding of mechanism of action on different diseases related to prognosis.

## Conclusion and Future Perspective

Endorphins are neuropeptide's produced from pituitary gland in response to pain and stress release CRH (corticotrophic releasing hormone) from hypothalamus activate HPA axis (hypothalamo pituitary adrenal axis) release cortisol and nor-adrenaline mediated activation of inflammatory mediators IL-1 $\beta$ , TNF- $\alpha$ , IL-6 from inflammatory cells activate NF-KB, STAT-3 transcription factors involved in tumor progression, auto-immune diseases, infectious diseases. Beta-endorphins is an abundant endorphin synthesized and stored in pituitary gland involved in immune stimulatory, anti-inflammatory, stress buster, analgesic activity in treatment of various diseases. It acts as a future preventive, promotive, therapeutic and palliative treatment of diseases and dose dependent action on prognosis of disease need to be known.

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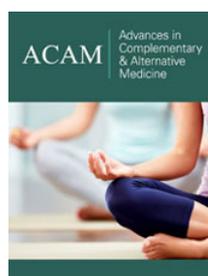
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