



A Genetic Study on Herbal Formulation's Approach to its Neuroprotective Antioxidant and Anti-Inflammatory Properties Against the Peroxidative DNA Damage and Apoptosis in Morphine Induced Sprague Dawley Rats: An Alternative Perspective

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ABSTRACT

*Morphine is the most widely used analgesic for pain control. It is a highly addictive narcotic drug used to relieve moderate to severe pain. It is derived from opium poppy *Papaver Somniferum* that binds to opiate receptors which directly changes the feelings of chronic morphine users. Morphine displays an effect on the mesolimbic pathway, resulting in an increase in dopamine levels which causes the activation of the reward system. Prolong use of morphine results in the craving of the drug. The individual then develops an addiction becoming dependent and then consumes opiates in excess to counteract the withdrawals when an absence of opiate occurs. A condition called morphine tolerance then develops. A higher dose of morphine is then needed to achieve the same analgesic effects due to the decrease of the drugs tolerance in a person. Chronic usage of morphine exhibits a few side effects including an increase in oxidative stress, cell apoptosis, neuronal dysfunction and toxicity. One of the mechanisms proposed that lead to withdrawal and dependency is caused by an accumulation of free radicals leading to the abundance of oxidative stress. This in turn will lead to neurotoxicity and cell death within the brain due to chronic morphine administration over a prolong period of time.*

Keywords: Adipokines; Phytosome; Banana peel; Phosphorus; Complement

INTRODUCTION

It has been previously found that abundant of u-opioid receptors found in the VTA regions of the brain. The activation of these receptors is depending on the rewarding effects by morphine similarly numerous studies demonstrated that the activation of dopaminergic neurons in the VTA regions of the brain is related to the addictive behaviours of a morphine dependent individual. Thus, one of the key factors in determining an addiction to an addictive substance could be the results from the activation of the VTA-dopaminergic neurons produced by morphine [1].

In addition, BDNF plays an important factor in neural reconstruction, brain growth as well as synapse plasticity BDNF receptors is copiously found in the VTA-dopaminergic neurons. BDNF could lead to protection and survival of the dopamine neurons found in the brain. Numerous studies have asserted that BDNF plays a role in memory,

learning, perception, identification, as well as regulation of different feelings. The disarranging of BDNF can cause various cognitive disorders such as addiction, anxiety disorders and etc. On the other hand Cyclic AMP response element binding protein (CREB) aids in the maturation of cell, more specifically in the survival, proliferation, neural formation, memory, learning and proliferation of cells. CREB is also recognized as a central protein that is found within the whole body and is identified as one of the transcription factors. Expression of BDNF gene is seen to be regulated by CREB. A decrease of inactivation of CREB may result in the reduction of BDNF gene expression.

In morphine dependent rats, BDNF gene expression levels have shown to decrease in VTA regions of the brain due to the decrease of CREB activity. Besides that, studies conducted by Yang et al., have concluded that CREB phosphorylation decreased in the hippocampus area of rats brains after chronic exposure to morphine. Zhou et al and Zhang et al both presented outcomes that the decrease of CREB levels in the Nucleus Accumbens as well as a significant reduction of CREB gene expression in the VTA regions in chronic morphine dependent rats [2].

Numerous researches have proven that consumption of polyphenols, an organic compound which is found abundantly in plants plays a key role in the modulation of chronic diseases, cell proliferation, weight and metabolism of cells (24). The effects of polyphenols have also been proven to show various properties such as anti-inflammatory and anti-oxidative. Therapeutically polyphenols display preventative effects on diseases such as neurodegenerative disorders, obesity, cardiovascular and cancer.

Plants such as *Musa Accuminata* (MA), *Centella Asiatica* (CA), *Barringtonia Racemosa* (BR) and *Olea Europea* (OE) oil, contains numerous polyphenols associated with the properties that is able to counteract free radicals and this results in preventing neurotoxicity and cell apoptosis. MA contains the polyphenol epigallocatechin gallate (EG). Through numerous findings, EG possesses therapeutic effects such as anti-oxidant properties, which act as radical scavengers that protect neurons, and inhibit neurotoxicity effects which is closely linked to neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease and Huntington's disease [3].

Anti-oxidant compounds, caffeic acid derivatives and flavanols are found within the leaf and roots of CA. This compound exhibits high anti-oxidant levels in aiming to reduce significantly the levels of oxidant such as malondialdehyde (MA). This supports the numerous findings of the neuroprotective properties of CA in the inhibition of free radical induced cell death and protective effects in diseases that exhibits beta-amyloid toxicity [4].

Recent studies have validated that BR, contains high levels of anti-oxidant properties such as phenolic and flavonoid acids, ethanolic acid, quercetin and kaemferol. Phenolic compounds encompass anti-inflammatory properties by rehabilitating the redox balance, which results in the reduction of oxidative stress. This is done by the alteration of the inflammatory responses resulting in the alleviation of the cytokine pathway. Flavonoids within BR function by counteracting free radicals and thus decreasing the risk of cancer development by influencing the growth of tumour cells [5].

CONCLUSION

The compound phenolic acid is found aplenty within the Olive oil tree. Oleuropein has been reported widely to poses numerous antioxidative, antimicrobial, antiviral, anti-inflammatory, cardioprotective and neuroprotective properties (38). Carotenoids and phenolic compounds found have revealed to be advantages in preventing diseases and also anti-aging properties (39-40). Its neuroprotective properties are able to prevent oxidative stresses caused by morphine which produces free radicals after prolong intake. Several phenolic compounds have proven to show positive outcome as a preventative and management of type 2 diabetes. This is a result of its protective effect of beta cells from toxicity caused by glucose. As a result, digestion of starch is reduced, the alteration and regulation of glucose promotes better glycaemic control.

Hence the purpose of this study is to determine the genetic effects of an herbal combination composing of *Musa Accuminata* (MA) Leaves, *Centella Asiatica* (CA) Leaves, *Barringtonia Racemosa* (BR) Leaves and *Olea Europea* (OE) Oil in counteracting the neurotoxicity, neurodegenerative and cell apoptosis of a morphine dependent individual.

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