Annual Research & Review in Biology
4(24): 4445-4449, 2014

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Pharmacological Properties of *Papaver rhoaes L.*

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Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

Review Article

Received 25th June 2014
Accepted 10th August 2014
Published 19th August 2014

ABSTRACT

The focus on herbal products for medicinal proposes has increased during the past decade. *Papaver rhoaes L*. (PR), commonly known as corn poppy, belongs to the *Papaveracea* family is used in southwestern Asia for some medicinal proposes. Modern pharmacology revealed that its extract contains several alkaloids such as rhoeadine, rhoeadic acid, papaveric acid, rhoeagenine, and anthocyanins. Studies in animal models have shown that PR extract can reduce morphine-induced place preference, sensitization, locomotor activity, and locomotor and pain tolerance. Furthermore, it has been shown that the extract also reduces stress-induced alterations in plasma corticosterone levels and induces analgesic and anti-inflammatory effects in mice. None clinical trial study finds for this plant. In conclusion, despite of lack in clinical trial studies, the existing evidence suggests that the PR extract possess medicinal properties and may be used as a therapeutic for drug addiction and pain and stress management.

Keywords: Papaver rhoaes; morphine dependence; pain; inflammation; stress.

1. INTRODUCTION

Papaver rhoaes L. is an annual herb commonly grown in several other parts of the world including Iran [1]. The flowers are red in color with a short life span and a capsule grows after the flowers hover [1]. The plant grows up to 25cm to 59cm in height [1]. The plant has

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been used for medicinal proposes a long time ago. For example, in Iranian folk medicine, the flowers of the plant are used to treat gastrointestinal discomforts [1]. In modern food industry, the fresh or dried flowers of the plant are used as ingredients in food preparations [2]. Pharmacological studies have shown that the plant extract may have some radical scavenging properties [3]. Investigations also indicated that the PR extract also possess antin-ulcergenic property [4]. Moreover, phytochemical analysis has revealed that the plant extract contains several alkaloids includingrhoeadine, rhoeadic acid, papaveric acid, rhoeagenine and anthocyanins [5-8]. It must be mentioned that toxicological study by Soulimani R and co-workers revealed that the plant extract has no toxic effects in mice, and perhaps in human as well [9]. Despite of studies using the plant extract effects in animal models, however, none clinical trial study were find. Here, we attempt to systematically review the existing literature on the pharmacological properties of PR extract.

1.1 Effects of the Hydro Alcoholic Extract of *Papaver rhoeas* on Locomotion

Studies on locomotion suggest that locomotor activity arises from dopamine neuron activity in the ventral tegmental area, nucleus accumbens and dorsal striatum [9]. Moreover, several neurotransmitters including acetylcholine [10] and glutamate [10] have been shown to affect the locomotion. PR extract has been shown to inhibit the effects of morphine on locomotor activity [11], behavioral sensitization [11] and behavioral tolerance [12] in mice in a dose-independent manner. The authors have postulated that the extract may have some ingredients with anti-dopaminergic, anti-glutamatergic, or anti-cholinergic properties which could be interacting with these neurotransmitters in various regions of the central nervous system. These studies were indicate that the plant extract with no effects on animals reward system, can interact with the psychostimulant properties of morphine and one may conclude that the plant extract may be useful for treatment of morphine-induced psycho stimulant effects in other animal models as well as in human.

1.2 Induction of Psychological Dependence by the Hydro Alcoholic Extract of *Papaver rhoaes*

Psychological dependence is defined as a desire for repeated use of abused drugs despite their adverse side effects. Psychological dependence is considered as the main reason for relapse to drug abuse [13]. Several animal models have been developed to study this phenomenon including conditioned place preference (CPP) and self-administration [14]. Studies using the place preference method have revealed that PR hydro alcoholic extract did not induce CPP in a procedure identical to that used for morphine [15]. However, it is interesting to note that the extract can inhibit the effects of morphine on both acquisition and expression of CPP [15]. Considering the findings of these studies, it is clear that the extract of the PR may be used as anti-euphoric drug in the human and we suggest that some clinical trials in this regard may be useful. It must be noted that since the biological properties of different abused drugs shown similarities [13], the effects of the extract on other abused drugs such as cocaine and nicotine may be similar to morphine.

1.3 Antinociception and Anti-inflammatory Effects of the *P. rhoaes* Extract

Pain is considered as an unpleasant sensation that occurs during and/or after tissue damage [16]. Pain relief is the subject of thousands of investigations around the world [16]. Research for antinociceptive and anti-inflammatory drugs with herbal origin has a long lasting history. Since PR belongs to the kingdom of herbs that are well known for their anti-inflammatory

properties, it was postulated that the extract of PR might also possess similar property. Experiments have shown that the extract not only inhibits both pain phases of formalin test, but can also inhibit inflammation induced by formalin [17]. These effects may be due to the activity of PR extract on opioid, glutamate, and nitric oxide systems [17]. In addition, PR extract has been shown to elevate plasma corticosterone concentration indicating that the anti-inflammatory effects of the extract can also be indirect [17]. Considering the fact that the PR extract did not induce dependence and addition in animal models [15], its anti-nociceptive properties is in the high value and some clinical trials in this regard may be useful. Even thought, it may open a new line of investigation in pain management and relief.

1.4 Stress Amelioration Properties of the *P. rhoaes* Extract

Stress is a physiological state of mind, which affects the body, thoughts, feelings, behavior and the quality of life [18]. Several researchers including psychologists and psychiatrists have been working to find methods to overcome the effects of stress [18]. However, stress amelioration still remains as one of the major problems [18]. Herbal medicine may serve as an alternate and promising therapeutic approach for stress related effects. Experiments with the extracts from PR have showed that the mice following treatment with the extract were able to tolerate intense stress without experiencing side effects such as increase in plasma corticosterone levels, reduction in food intake, and anorexia, suggesting the extract may protect against stress related effects [19]. The interesting property of the PR extract for ameliorating the stress effects may help the psychologists, psychiatrists and other health professionals dealing with stress and stress amelioration for pharmacological stress management which still remain as one key stones in health management. In addition, fractional extraction can further help us for better understanding of the extract pharmacognosy.

1.5 Effects of *Papaver rhoaes* Extract on Stress-Induced Learning and Memory Impairment

Stress has been known to cause impairment in learning and memory in human and animal models [20]. It has been postulated that corticosterone (stress hormone) released during stress affects hippocampal neurons by binding to its receptor located on the cell body [21]. PR extract has been shown to improve stress-induced memory impairment in mice [22]. However, the extract did not reducestress-induced learning impairment in animals [23]. As noted in the previous section, the extract may be useful for stress management and reliving its side effects. Perhaps one of the important side effects of the chronic stress is memory decline which can extending to improper decision making. However, other possibilities including brain shrinkage also may be occurred [21]. Considering the fact that stress hormones including corticosterone may have a role in this phenomenon [21], it can be concluded that the extract may be an excellent choice for protecting the brain against stress.

2. CONCLUSION

The research discussed in this review shows that the hydro alcoholic extract of *Papaver rhoaes* interact with several aspects of morphine including CPP, behavioral sensitization and tolerance, and dependence. In addition, PR extract has also been shown to interact with signaling mechanisms activated during stress and ameliorates stress related side effects. Future studies should investigate in detail about the molecular mechanisms to develop therapeutics based on PR extract for drug abuse and pain and stress related treatment.

However, due to poor clinical studies in this regard, we propose that some clinical trials also must be down for clinical usage of the PR extract in human as well.

ACKNOWLEDGEMENT

This work was supported by a grant from Neuroscience Research Center, Baqiyatallah University of Medical Science.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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