



دانشگاه علوم پزشکی
و خدمات بهداشتی درمانی کرمان

دانشکده طب ایرانی

پایان نامه مقطع دکتری تخصصی طب سنتی ایرانی

عنوان

بررسی اثر فرآورده سنتی بر پایه اسپند بر نشانه‌های ترک اعتیاد در موش‌های صحرایی نر
وابسته به مورفین و متادون

توسط

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**Kerman University of
Medical Science
Faculty of Persian Medicine**

In Partial Fulfillment of the Requirements for the Degree Ph.D.

Title

**Effect of the traditional preparation based on *Peganum harmala*
on morphine and methadone withdrawal signs in male Wistar rats**

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Thesis No: **21**

Date: **July 2021**

چکیده

مقدمه و اهداف: اعتیاد به مواد افیونی یکی از معضلات عمده بهداشتی و اجتماعی در کشورهای در حال توسعه محسوب می‌شود. با توجه به ارزان تر بودن فرآورده‌های گیاهی، مقبولیت بیشتر در اجتماع، در دسترس تر بودن و نیز با توجه به عوارض کمتر، این داروها می‌توانند به‌عنوان یک گزینه درمانی مکمل برای ترک مواد افیونی مطرح گردد. لذا این مطالعه باهدف بررسی اثر فرآورده سنتی بر پایه اسپند بر علائم رفتاری و مکانیسم‌های احتمالی آن در موش‌های معتاد به مورفین و متادون در مقایسه با گروه کنترل انجام گرفت.

روش‌ها: ۱۱۲ موش صحرایی نر نژاد ویستار به‌طور تصادفی به ۱۶ گروه هفت‌تایی تقسیم شدن دو در دودسته قرار گرفتند. گروه‌های دسته اول به مدت یک هفته نرمال سالین، کربوکسی متیل سلولز، مورفین تزریقی به‌تنهایی و یا مورفین تزریقی به همراه فرآورده سنتی خوراکی در دوزهای $1/4 \text{ mg/kg}$ و mg/kg $2/8$ به‌صورت تک‌دوز یا روزانه دریافت کردند. گروه‌های دسته دوم شامل دریافت‌کننده پنج هفته نرمال سالین یا کربوکسی متیل سلولز و دریافت‌کننده یک هفته مورفین تزریقی و سپس چهار هفته گاوژ متادون به‌تنهایی یا به همراه $2/8 \text{ mg/kg}$ فرآورده سنتی خوراکی به‌صورت تک‌دوز یا روزانه بود. آزمون‌های رفتاری، نشانه‌های ترک القاشده با نالوکسان و همچنین پارامترهای نوار قلب، تست‌های آنتی‌اکسیدانی (شامل محتوای سرمی مالون‌دی‌آلدهید، متابولیت‌های پایدار نیتریک اکسید و ظرفیت تام آنتی‌اکسیدانی) و فاکتورهای ارزیابی کبدی بررسی شد. علاوه بر این، بیان پروتئین *c-fos* توسط وسترن بلات ارزیابی گردید.

یافته‌ها: فرآورده سنتی بر پایه اسپند در آزمون رفتاری ترجیح مکان شرطی شده، سبب کاهش معنی‌دار اثر پاداش مورفین گردید. پاسخ مشابهی در مورد متادون نیز مشاهده شد. علاوه بر آن فرآورده سنتی در موش‌های صحرایی وابسته به مورفین و متادون به ترتیب منجر به کاهش فعالیت حرکتی و اضطراب قابل توجهی گردید. اما دریافت فرآورده سنتی تغییر فراوانی در حافظه عملکردی ایجاد نکرد. فرآورده سنتی همچنین کاهش بارزی در نشانه‌های ترک القاشده با نالوکسان ایجاد نمود. این فرآورده سبب افزایش ظرفیت تام آنتی‌اکسیدانی و کاهش متابولیت‌های پایدار نیتریک اکسید در موش‌های وابسته به مورفین و کاهش محتوای سرمی مالون‌دی‌آلدهید در موش‌های وابسته به متادون گردید. ارزیابی‌های کبدی نشان داد دریافت

روزانه فرآورده سنتی می‌تواند SGPT، آلکالین فسفاتاز و بیلی‌روبین مستقیم را در موش‌های وابسته به متادون کاهش دهد. علاوه بر آن بیان پروتئین *c-fos* در موش‌های وابسته به مورفین و متادون با دریافت فرآورده سنتی کاهش یافت. به جز افزایش تعداد ضربان قلب در گروه دریافت‌کننده دوز بالای فرآورده سنتی، تغییر معناداری در پارامترهای نوار قلب مشاهده نشد.

نتیجه‌گیری: فرآورده سنتی بر پایه اسپند می‌تواند علاوه بر کاهش نشانه‌های ترک متادون و مورفین، تأثیرات مثبتی بر برخی از فاکتورهای ارزیابی کبدی، تست‌های آنتی‌اکسیدانی و مولکولی در موش صحرائی داشته باشد؛ بنابراین پیشنهاد می‌شود به‌عنوان یک گزینه مکمل برای درمان اعتیاد در مطالعات بالینی آینده مورد بررسی قرار گیرد.

کلمات کلیدی: اسپند؛ اعتیاد؛ مورفین؛ متادون؛ طب سنتی

Abstract

Introduction and objectives: Opioid addiction is one of the major health and social problems in developing countries. Due to the cheapness of herbal products, more acceptance in the community, more availability and also due to less side effects, these drugs can be considered as a complementary treatment to quit opioids. Therefore, the aim of this study was to investigate the effect of the traditional preparation based on *Peganum harmala* on morphine withdrawal signs and evaluation of its probable mechanisms in male Wistar rats in comparison with the control group.

Methods: 112 male Wistar rats were randomly divided into 16 groups of seven and divided into two categories. First category groups received normal saline, carboxymethylcellulose, subcutaneous morphine alone or in with a traditional oral preparation in doses of 1.4 mg/kg and 2.8 mg/kg as a single or daily dose. The second category consisted of receiving five weeks of normal saline or carboxymethylcellulose and one week receiving subcutaneous morphine and then four weeks of methadone gavage alone or with 2.8 mg/kg of traditional oral preparation as a single dose or daily. The behavioral tests, naloxone-precipitated withdrawal signs as well as ECG parameters, antioxidant tests (including serum malondialdehyde content, stable metabolites of nitric oxide, and total antioxidant capacity) and liver function tests were investigated. In addition, c-fos protein expression was assessed by Western blotting.

Results: The traditional preparation based on *P. harmala* significantly reduced the effect of morphine reward in the conditioned place preference test. A similar response was observed with methadone. In addition, the traditional preparation significantly reduced locomotor activity and anxiety in morphine and methadone-dependent rats, respectively. But receiving the traditional preparation did not significantly alter functional memory. The traditional product also significantly reduced naloxone-precipitated withdrawal signs. The traditional preparation increased total antioxidant capacity and decreased stable

metabolites of nitric oxide in morphine-dependent rats and decreased serum malondialdehyde content in methadone-dependent rats. The liver function tests showed that daily dose of traditional products could reduce SGOT, SGPT, alkaline phosphatase and direct bilirubin in methadone-dependent rats. In addition, c-fos protein expression was reduced in morphine and methadone-dependent rats with the traditional preparation. Except for the increase in heart rate in the group receiving the high dose of traditional preparation, no significant change was observed in the parameters of the ECG.

Conclusion: In addition to reducing the signs of methadone and morphine withdrawal, the traditional preparation based on *P. harmala* could have positive effects on some liver function, antioxidant and molecular tests in rats; Therefore, it is suggested that it be considered as a complementary option for the treatment of addiction in clinical trials.

Keywords: *Peganum harmala*; Addiction; Morphine; Methadone; Traditional Persian Medicine

فهرست مندرجات

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چکیده

فصل اول: مقدمه و اهداف

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فصل دوم: بررسی متون

۱-۲- تعریف و کلیات ERROR! BOOKMARK NOT DEFINED.

۲-۲- اسپند .. *Peganum harmala* L. ERROR! BOOKMARK NOT DEFINED.

۳-۲- شقاقل *Malabaila secacul* Boiss. ERROR! BOOKMARK NOT

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۵-۲- متادون ERROR! BOOKMARK NOT DEFINED.

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فصل سوم: مواد و روش‌های تحقیق

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فصل چهارم: یافته‌ها

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فصل پنجم: بحث و نتیجه‌گیری

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دانشگاه علوم پزشکی کرمان
مدیریت تحصیلات تکمیلی دانشگاه

بسمه تعالی

صور تجلسه دفاع از پایان نامه

جلسه دفاعیه پایان نامه تحصیلی آقای دکتر محمد علی احمدیان مقدم دانشجوی دکتری تخصصی (Ph.D) رشته طب سنتی ایرانی دانشکده طب سنتی ایرانی دانشگاه علوم پزشکی کرمان تحت عنوان « بررسی اثر فرآورده سنتی بر پایه اسپند بر نشانه‌های ترک اعتیاد در موش‌های نر صحرایی وابسته به مورفین و متادون » در ساعت ۸ روز سه شنبه مورخ ۱۴۰۰/۰۴/۲۹ با حضور اعضای محترم هیات داوران به شرح ذیل:

امضا	نام و نام خانوادگی	سمت
	۱- سرکار خانم دکتر مهرداد مهربانی ۲- جناب آقای دکتر محمد هادی نعمت الهی ۳- سرکار خانم دکتر میترا مهربانی	الف: استادان راهنما
	۱- جناب آقای دکتر نوذر نخعی ۲- جناب آقای دکتر ایمان فاطمی	ب: استادان مشاور
	جناب آقای دکتر غلامرضا اسدی کرم	ج: عضو هیات داوران (داخلی)
	سرکار خانم دکتر آزاده امین زاده	ج: عضو هیات داوران (داخلی)
	سرکار خانم دکتر زرین سرحدی نژاد	ج: عضو هیات داوران (داخلی)
	جناب آقای دکتر محمد شعبانی	ج: عضو هیات داوران (داخلی)
	جناب آقای دکتر حسین کارگر	ج: عضو هیات داوران (داخلی)
	سرکار خانم دکتر زهره سرحدی نژاد	د: عضو هیات داوران (خارجی)
	جناب آقای دکتر محمد ستایش	ه: نماینده تحصیلات تکمیلی

تشکیل گردید و ضمن ارزیابی به شرح پیوست با درجه عالی و نمره ۱۸٫۹۶ مورد تأیید قرار گرفت.

مهر و امضاء معاون آموزشی

