

学校编码：10384

分类号\_\_\_\_\_密级\_\_\_\_\_

学号：24520141153582

UDC\_\_\_\_\_

廈門大學

硕士学位论文

柴郁地仙方抗围绝经期抑郁症  
作用机制研究

Research on the Anti-perimenopausal Depression

Mechanism of Chaiyu Dixian Prescription

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论文提交日期：2017年4月

论文答辩时间：2017年5月

学位授予日期：2017年6月

答辩委员会主席：\_\_\_\_\_

评阅人：\_\_\_\_\_

2017年04月

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## 摘要

### 目的:

1. 观察卵巢去势手术与慢性轻度不可预见性应激对大鼠的影响,探讨围绝经期抑郁症的发作与生理因素、环境应激的关系。

2. 观察柴郁地仙方对围绝经期抑郁症模型大鼠的药理效应;从单胺类神经递质、HPO轴及血清微量元素方面探讨柴郁地仙方抗围绝经期抑郁症作用机制。

### 方法:

通过对健康成年雌性大鼠行双侧卵巢去势手术建立内源性雌激素撤退围绝经期模型,在此基础上通过孤养及21天慢性轻度不可预见性应激复制大鼠抑郁模型。实验动物分为假手术组、去势组、模型组、氟西汀组、雌二醇组、柴郁地仙方组,应激过程给药23天。通过大鼠体质量、敞箱实验得分及糖水消耗量评价大鼠行为学变化;采用ELISA法检测大鼠血清 $E_2$ 、FSH、LH、GnRH及下丘脑5-HT、NE、DA的含量;采用络合比色法检测血清Zn、Cu含量。

### 结果:

1. 与假手术组比较:模型组大鼠敞箱实验水平得分、探索得分、24小时糖水消耗量、体质量变化率低下,血清 $E_2$ 、Zn及下丘脑5-HT、NE、DA含量下降,血清FSH、LH、GnRH、Cu含量升高( $P<0.05$ ,  $P<0.01$ );去势组大鼠敞箱实验水平得分、24小时糖水消耗量低下,体质量变化率升高,同时出现血清 $E_2$ 含量低下及FSH、LH、GnRH含量升高( $P<0.05$ ,  $P<0.01$ ),但敞箱实验探索得分、下丘脑5-HT、NE、DA含量及血清Zn、Cu水平无明显改变( $P>0.05$ )。

2. 柴郁地仙方对模型大鼠具有维持敞箱实验得分、24小时糖水消耗量、体质量变化率正常,上调血清 $E_2$ 、Zn及下丘脑5-HT、NE、DA含量,抑制血清FSH、LH、GnRH、Cu过渡分泌的作用( $P<0.05$ ,  $P<0.01$ )。

### 结论:

1. 卵巢功能缺失能够影响大鼠行为及HPO轴功能,使其出现类抑郁样变化,但不足以导致其出现单胺类神经递质与微量元素的异常分泌,提示围绝经期抑郁症的发生不单纯是卵巢功能衰退的结果,更与长期的环境应激相关。

2. 柴郁地仙方能够维持围绝经期抑郁症模型大鼠自主活动、探索行为、快感及体质量增长的正常，其作用机制与调节 HPO 轴的紊乱、上调单胺类神经递质含量及纠正血清 Zn、Cu 异常分泌相关。

**关键词：**柴郁地仙方；围绝经期；抑郁症；动物实验

厦门大学博硕士论文摘要库

## Abstract

### Objective:

1. Observe the effects of ovariectomy surgery and chronic mild chronic stresses (CUMS) in rats, to explore the relationship between environmental stresses, physiological factors and the emergence of perimenopausal depressive disorder.

2. Observe the pharmacological effect of using Chaiyu Dixian Prescription to treat rats with perimenopausal depressive disorder; to investigate the mechanism of action using Chaiyu Dixian Prescription to anti-perimenopausal depression from monoamine neurotransmitter system, the Hypothalamus-pituitary-ovary axis and trace elements in serum.

### Method:

Experiments using ovariectomy surgery established the endogenous estrogen withdraw model, simulating the status of menopausal women with low ovarian function, on this basis, using feeding alone and 21 days' CUMS replication rat model of depression. The experimental animals were divided into 6 groups, sham operation group, ovariectomized group, model group, Fluoxetine group, Estradiol group, Chaiyu Dixian I Prescription, intragastric administrating 23 days. Observe the behavioral changes of rats with the change of body weight, the scores of open-field test (OFT) and the sucrose water consumption experiment; Detecting serum E<sub>2</sub>, FSH, LH, GnRH's level and hypothalamic 5-HT, NE, DA's content by Elisa, colorimetric methods were used to examine serum copper ion (Cu), zinc ion (Zn)'s content.

### Results:

1. Compared with sham operation group, the model group rat's level and exploratory scores in the OFT, consumption of sucrose solution, the rate of weight change, serum E<sub>2</sub>, Zn, hypothalamic 5-HT, NE, DA reduced, serum FSH, LH, GnRH, Cu increased ( $P < 0.05$ ,  $P < 0.01$ ); the ovariectomized group rat's level scores in the OFT, consumption of sucrose solution, serum E<sub>2</sub> reduced, the rate of weight change, serum FSH, LH, GnRH increased ( $P < 0.05$ ,  $P < 0.01$ ), but there was no significant

difference between the exploratory scores in the OFT, hypothalamic 5-HT, NE, DA, serum Cu, Zn ( $P>0.05$ ).

2. Chaiyu Dixian Prescription could increase perimenopausal depressive disorder model rat's level and exploratory scores in the OFT, consumption of sucrose solution, the rate of weight change, serum  $E_2$ , Zn, and hypothalamic 5-HT, NE, DA, reduce its serum FSH, LH, GnRH and Cu ( $P<0.05$ ,  $P<0.01$ ).

**Conclusion:**

1. Ovarian dysfunction can affect rat's behavior and function of the Hypothalamus-pituitary-ovary axis, ovariectomy surgery can lead to depression-like behavioral changes, nevertheless, but cannot affect rat's monoamine neurotransmitter system and trace elements in serum. These results suggested that long-range environmental stress has more influence meaning than ovarian function decline in the occurrence of perimenopausal depressive disorder.

2. Chaiyu Dixian Prescription has the effects keeping model rat's spontaneous activity, exploratory behavior, pleasant sensation and normal weight gain. The mechanism of action of Chaiyu Dixian Prescription's anti-perimenopausal depression effect relating with regulate the function of HPO axis, increase the monoamine neurotransmitters of hypothalamus' content and improve Zn deficiency.

**Keywords:** Chaiyu Dixian Prescription; Perimenopause; Depression; animal experiment

## 英文缩略词表

缩写名	英文名	中文名
FSH	Follicle-Stimulating Hormone	促卵泡生成素
VMS	Vasomotor Symptoms	血管舒缩症状
PDD	Permenopausal Depressive Disorder	围绝经期抑郁症
ERT	Estrogen Replacement Therapies	雌激素替代疗法
HRT	Hormone Replacement Therapy	激素替代疗法
GnRH	Gonadotropin Releasing Hormone	促性腺激素释放激素
STAR*D	Sequenced Treatment Alternatives to Relieve Depression	抗抑郁序贯疗法
HPA 轴	the Hypothalamic-Pituitary-Adrenal axis	下丘脑-垂体-肾上腺轴
HPO 轴	the Hypothalamic-Pituitary-Ovary axis	下丘脑-垂体-卵巢轴
E <sub>2</sub>	17 $\beta$ -estradiol	雌二醇
5-HT	Serotonin/ 5-hydroxytryptamine	5-羟色胺
ELISA	Enzyme Linked Immunosorbent Assay	酶联免疫吸附测定
NE	Norepinephrine	去甲肾上腺素
DA	Dopamine	多巴胺
LH	Luteinizing Hormone	促黄体生成素
SHAM	Sham operation	假手术
OVX	Ovariectomy	卵巢去势
CUMS	Chronic Unpredictable Mild Stress	慢性轻度不可预见性应 激
OFT	Open-Field Test	敞箱实验
SSRI	Selective Serotonin Reuptake Inhibitor	5-羟色胺再摄取抑制剂
CDP	Chaiyu Dixian Prescription	柴郁地仙方



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