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Hans汉斯

中药防治抑郁症的研究进展

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摘　要

抑郁症是一种常见且严重的精神疾病，临床表现为情绪低落、思维迟缓、意志活动、减退嗜睡、食欲减退、疲劳乏力、性欲减退、失眠等，甚者自杀。其患者的功能残疾程度高于糖尿病、高血压、冠状动脉疾病或关节炎等慢性疾病患者。预计到2030年抑郁症成为世界第二大疾病。目前抑郁症的发病机制尚未定论。临床以西药为主的抗抑郁药，出现时效长，疗效差，副作用明显等问题。而中药在中医辨证与整体的指导思路下，因多靶点、多途径、整体调节且不良反应小的特点，医生和患者逐渐接受中医药治疗。本文主要探讨抑郁症在常用中药的组方、单药和中药提取化合物的治疗方面的研究进展，为未来对其进行深入研究可为抗抑郁治疗提供新思路。

关键词

抑郁症，中药，机制

Research Progress of Depression Prevention and Treatment with Chinese Medicine

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Abstract

Depression is a common and serious mental disease, with clinical manifestations such as de-

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pressed mood, slow thinking, willpower activity, decreased drowsiness, decreased appetite, fatigue, decreased libido, insomnia, and even suicide. Their patients had a higher degree of functional disability than those with chronic conditions such as diabetes, hypertension, coronary artery disease or arthritis. Depression is expected to become the world's second largest disease by 2030. At present, the pathogenesis of depression has not yet been determined. Antidepressants, which are mainly western medicine in clinic, have such problems as long time effect, poor curative effect, obvious side effects, etc. Under the guidance of TCM syndrome differentiation and holism, doctors and patients of traditional Chinese medicine (TCM) are gradually receiving TCM treatment due to the characteristics of multiple targets, multiple pathways, overall regulation and small adverse reactions. This paper mainly discusses the research progress of depression in the treatment of commonly used traditional Chinese medicine (TCM) formula, single drug and Chinese medicine extract compounds, to provide new ideas for further research and antidepressant treatment in the future.

Keywords

Depression, Traditional Chinese Medicine, Mechanism

1. 引言

抑郁症以显著而持久的心境低落为主要临床特征[1]。作为世界最常见的疾病之一，其发病率每年倍增，在中国，抑郁症被认为导致残疾的第二大原因[2]，由于女性生理、生殖结构和社会压力的问题，女性成为当代抑郁症的主要人群，每 10 个女性就有 3 个患有抑郁症[3]。尤其是围产期抑郁症发病率极高且对女性健康危害极大[4]。在性别化的社会化的进程中男性表达抑郁的方式与女性不同，虽然被诊断患有抑郁症的比例是女性的一半，但死于自杀的频率却是女性的 3 到 4 倍[5]，而青少年抑郁症[6]和老年人抑郁症[7]也逐渐成为当今的社会问题。通常抑郁症常与失眠相互交联，导致病情经久不愈。最新研究结果表明，抑郁症的特殊面容的敏感性会根深蒂固地影响患者的正常社会功能[8]。一项横断面研究调查了来自中国 194 个城市的 1210 名成年人，发现 53.8%的受访者将疫情的心理影响评价为中度或重度。16.5%的人报告有中度至重度抑郁症状，28.8%的人报告有中度至重度焦虑症状，8.1%的人报告有中度至重度压力水平。当前抑郁症致病机制尚且不明，主流假说有：单胺假说、神经内分泌失调、神经营养发育假说、免疫反应与神经炎症假说、微生物－脑－肠轴假说、下丘脑－垂体－肾上腺轴假说等假说[9]。而如今中医药在抑郁症上的治疗有多种优势成为当前抑郁症治疗的新潮。

2. 抑郁症机制

2.1. 单胺假说

经研究发现在抑郁症患者脑中的某些神经递质含量较低，导致位于上游神经元释放的神经递质较少，位于下游的神经元所接收到的神经递质减少而受到影响。这些神经递质通常是：5-羟色胺－成瘾和强迫行为；多巴胺－参与奖赏和惩罚的调节；去甲肾上腺素－维持睡眠与觉醒，由于这三种神经递质都有一个“氨基”基团所以也称“单胺假说”[10]。基于此假说的治疗则是提高脑内神经递质含量，有的靶向神

经元，使其产生更多的神经递质，也有靶向神经递质，使其在脑内不会快速降解掉。

最新的单胺假说是包括下调和脱敏的突触后去甲肾上腺素和 5-羟色胺受体，由于中枢神经系统突触间隙单胺类神经递质浓度水平或功能下降导致的，分别导致抗抑郁药的延迟治疗作用[11]。然而，在早期的研究中显示，长期的抗抑郁药物治疗可以下调去甲肾上腺素和 5-羟色胺的受体位点的密度通过长期抗抑郁治疗，也有学者提出了受体敏感性假说[12]。这一假说表明，长期的抗抑郁药物治疗可增加突触后 5-羟色胺的功能 1A 海马体中的受体。根据治疗的类型，他们认为这可能是通过突触后 5-羟色胺的敏感性增加而发生的 1A 受体或 5-羟色胺自身受体的脱敏。这个假设的一个问题是直接作用的 5-羟色胺 1A 受体激动剂并不是明显有效的抗抑郁药，并且增加了 5-羟色胺神经传递可能是必要的，但对抗抑郁疗效的不足。此外，这些受体现在可以通过注射特异性激动剂和测量特异性的神经内分泌反应，如催乳素水平的升高，这些结果表明这些受体的敏感性降低(见图 1)。

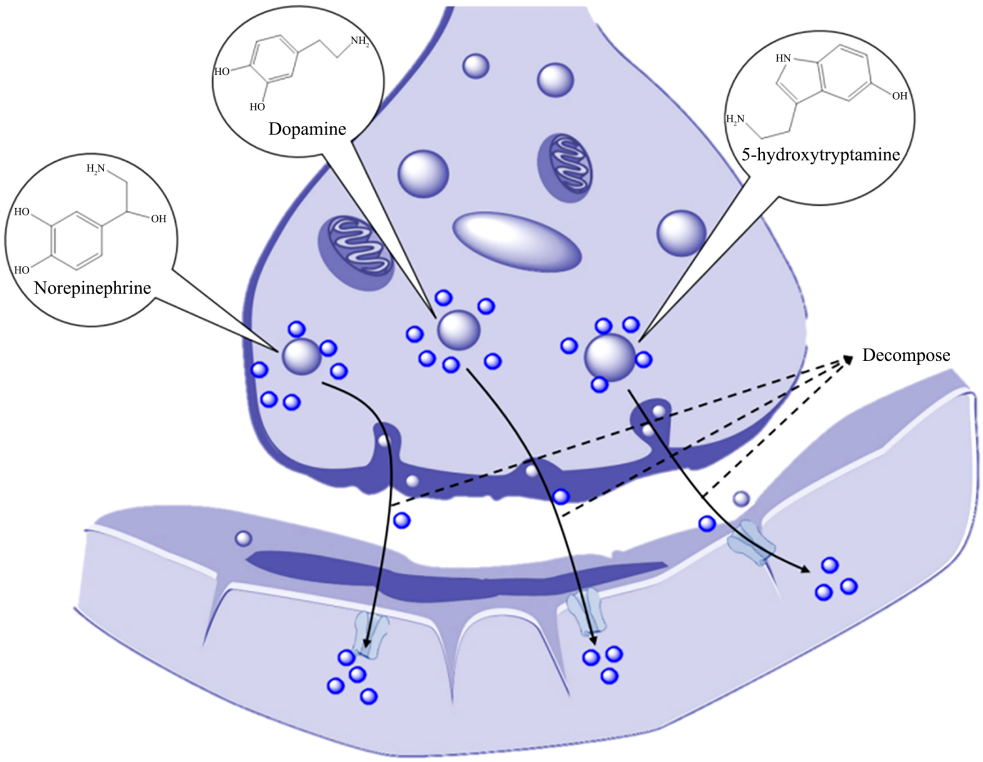

Figure 1. Monoamine hypothesis
图 1. 单胺假说

2.2. 免疫反应与神经炎症假说

炎症或炎症反应是免疫系统激活的结果，是指具有血管系统的活体组织对生物、物理、化学等损伤因子刺激所产生的防御[13]，而神经炎症则是外周分子通过血脑屏障[14] (blood-brain barrier, BBB)渗漏进入大脑，或者通过白细胞介素-1α (interleukin-1α, IL-1α) [15]等介质的饱和运输最后影响中枢神经系统。

小胶质细胞在正常的生理环境下，起着营养神经的作用，当受外界环境刺激的时候，小胶质细胞怎会被激活而分泌一系列炎症介质[16] (细胞因子和趋化因子)来抵抗外界危险刺激，产生免疫反应(见图 2)。而长期的炎症因子的刺激，会形成海马区神经元缺失及胶质细胞增生，最后导致抑郁行为。

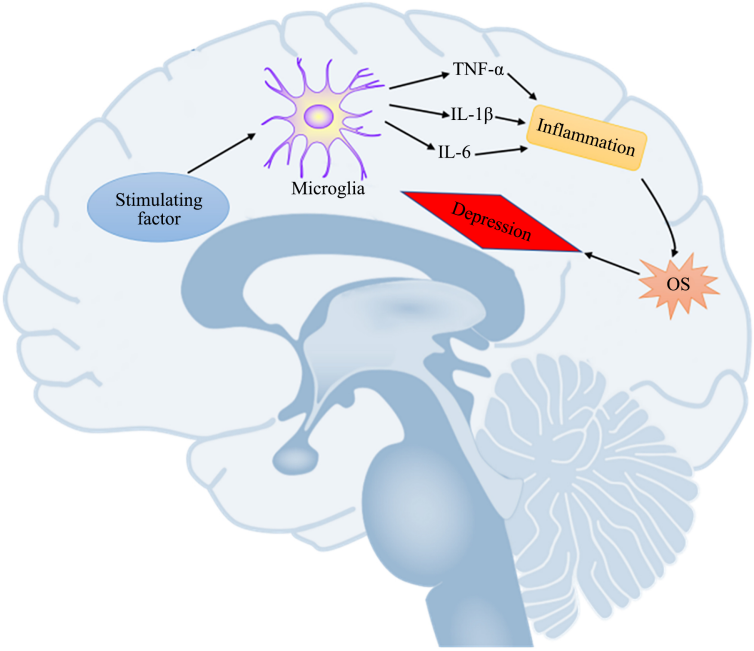

Figure 2. Neuroinflammation hypothesis
图 2. 神经炎症假说

2.3. 抑郁症与微生物－脑－肠轴假说

越来越多的证据揭示了肠道菌群在抑郁发病机制中的重要性，微生物－脑－肠轴假说也是目前研究抑郁症的新潮流。肠道菌群产生的代谢物参与神经递质的合成过程、前额皮质神经元的髓鞘化，以及杏仁核和海马的发育。一些细菌已被观察到产生神经调节物质，如动物神经系统中发现的：乙酰胆碱、多巴胺、血清素、GABA、去甲肾上腺素[17]。

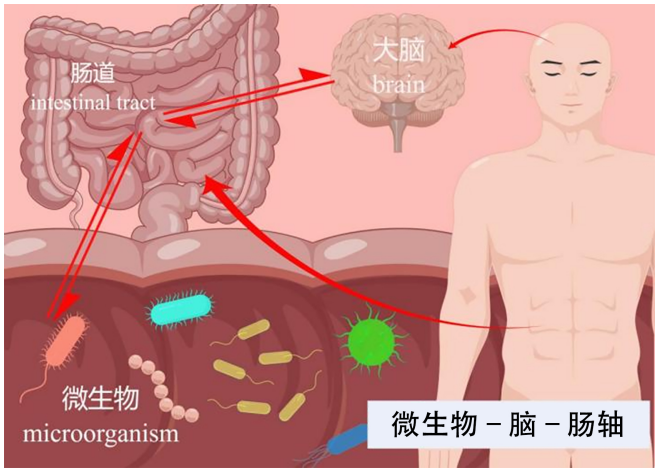

Figure 3. Microorganism-brain-intestine axis hypothesis
图 3. 微生物－脑－肠轴假说

每个个体的微生物群的组成都是独特的，是肠道环境、生活方式、饮食习惯等各种因素变化导致的结果。肠道菌群有代谢功能、营养功能和保护功能三大类[18]。代谢功能则是通过分解未消化的食物残渣

和生产维生素 B 和维生素 K 来实现的。营养功能包括通过参与肠细胞成熟和交换相关的过程来控制肠上皮的紧密性，而微生物群在活性方面的相互作用是胃肠道(GI)运动技能功能的另一个表现。而肠道细菌也是维生素的来源，包括维生素 K-2 和 B 族维生素(烟酸、生物素、叶酸和焦氧化定)。研究表明，抑郁症患者的血清中叶酸水平较低[19]。

免疫系统在肠道微生物对宿主系统特别是中枢神经系统功能的影响中起中介作用，肠道微生物组的每一种排列都会导致微生物产生脂多糖(LPS)，进而激活炎症反应而产生的细胞因子向迷走神经发送信号，从而连接下丘脑轴，导致神经系统炎症，而神经系统炎症反过来也激活了小胶质细胞，最后导致抑郁行为[20] (见图 3)。且肠道微生物群也被证明与细胞和发育生物学中的色氨酸前沿有关，肠道微生物群为改变大脑中的神经递质调节和治疗焦虑和抑郁等肠脑轴疾病提供了一种新方法。

2.4. 神经营养发育假说

据研究，在抑郁症患者死后的大脑样本中发现，BDNF (brain-derived neurotrophic factor 脑源、性神经营养因子)的 RNA (Ribonucleic Acid 核糖核酸)和蛋白质的水平下降，尤其是海马和杏仁核[21]。而在服用抗抑郁药物治疗后的抑郁症患者的脑内 BDNF 的表达则会增加。表明 BDNF(脑源性神经营养因子)及其受体 TrkB (神经营养受体酪氨酸激酶 2)与抗抑郁作用有关[22] (见图 4)。

BDNF (脑源性神经营养因子)是成人大脑中最丰富的神经营养因子，通过树突棘形态形成和树枝化调节神经元可塑性是大脑中活动神经元可塑性的关键中介物[23]，它对神经元的形态和生理有重要影响，增加了神经突起的发芽和突触的稳定，促进了长期增强。反之，BDNF 的合成和释放受神经元活性的调节。因为皮质 BDNF 是血清 BDNF 的主要来源，血清 BDNF 水平部分反映了其中枢神经系统的表达水平。在研究中发现 BDNF 在抑郁患者的血清中减少，在抗抑郁治疗时增加[24]。所以，在抗抑郁治疗中，关注 BDNF 是必不可少的。

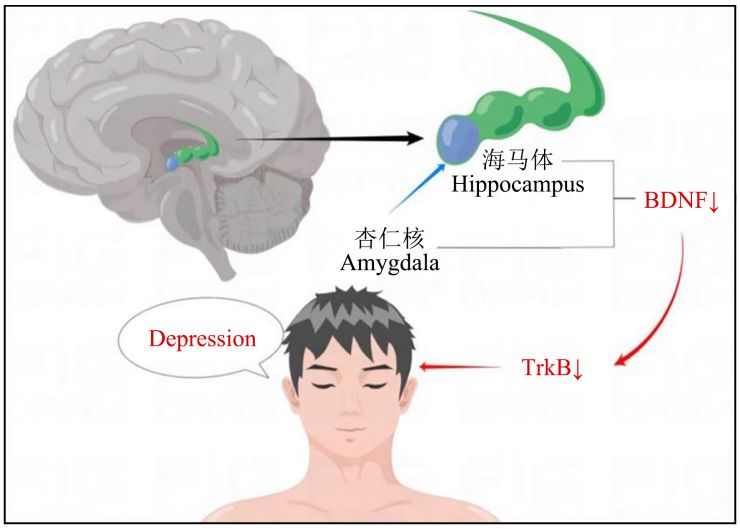

Figure 4. Neurotrophic development hypothesis
图 4. 神经营养发育假说

2.5. 下丘脑－垂体－肾上腺轴假说

HPA 轴是指的下丘脑－垂体－肾上腺轴，下丘脑－垂体－肾上腺轴从上到下是依次的促进下一个靶器官的激素分泌，反过来从下到上是依次的反馈性的抑制上一个激素的分泌，所以下丘脑－垂体－肾上

腺轴是一个神经内分泌反馈调节系统的轴，也叫 HPA 轴[25] (见图 5)。所以当 HPA 轴系统调节能力下降时就会导致抑郁行为。下丘脑旁室和垂体前叶以及肾上腺皮质三个器官组成，从上到下的一个无形的轴，可以对人体发挥非常重要的作用，其中最重要的作用就是由下丘脑所分泌的促肾上腺皮质激素释放激素，作用于垂体前叶来分泌促肾上腺皮质激素，促肾上腺皮质激素又作用于外周的肾上腺皮质，来刺激肾上腺分泌皮质醇，也就是常说的糖皮质激素，从而使糖皮质激素分泌到血液当中，去发挥强大的生理的重要的作用[26]。如果外周的肾上腺糖皮质激素分泌的浓度过高，就会反馈性地抑制垂体的促肾上腺皮质激素，和下丘脑的促肾上腺皮质激素释放激素的分泌减少，这就是 HPA 轴的抑制作用。正常人抑制作用和正向促进的作用，处在一种动态平衡，符合生理的需要。一个有机体应对压力体验的能力取决于其适当参与中枢和外周系统的 HPA 轴的能力，是用来适应不断变化的环境需求。HPA 轴是对压力的神经和行为反应的主要神经内分泌介质，该系统的功能障碍与发生精神健康障碍如抑郁、焦虑和创伤后应激障碍的风险增加有关[27]。所以，当 HPA 轴的调节失调，则会出现抑郁行为。

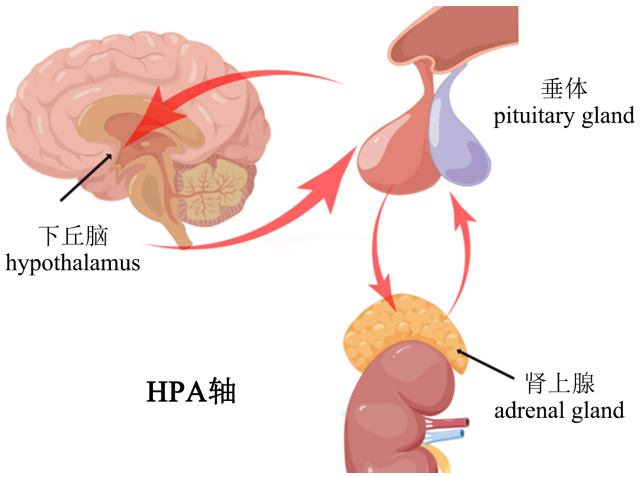

Figure 5. Hypothalamic-pituitary-adrenal axis hypothesis
图 5. 下丘脑－垂体－肾上腺轴假说

2.6. 基因－环境－表观遗传互做假说

表观遗传学的概念产生于 20 世纪 40 年代，生物学家康拉德·沃丁顿(Conrad Waddington)描述了基因和环境之间的相互作用。而现在表观遗传学事件被定义为：表观遗传学指的是在不改变原始序列的情况下对 DNA 转录的调控，受 DNA 甲基化、组蛋白修饰和非编码的控制[28]。表观遗传机制考虑个体遗传和环境因素之间的相互作用，分析这一过程为细胞内遗传物质表达的变化，这最终决定了个体表现出的特征。表观遗传学机制主要涉及生物体的生物学决定在其发展过程中更新和表达的方法和过程[29]。表观遗传机制在抑郁症和童年逆境患者中起作用的证据是，在这些人的大脑和白细胞中发现了表观遗传标记的增加和滥用物质似乎涉及 DNA、组蛋白或 microRNA 上的病理表观遗传标记的积累。DNA 的表观遗传改变，即基因表达，可由于不同的过程发生，如磷酸化、乙酰化和甲基化。DNA 甲基化是该领域研究最多的表观遗传学机制之一，通常包括在 DNA 的特定区域添加一个化学元素(甲基)。根据目前的假设，甲基化在胚胎阶段和整个发育过程中是一个常见的过程，其主要后果是沉默 DNA 的特定区域，阻止了将其激活的蛋白质的合成。因此，这种表观遗传机制将在该 DNA 区域的蛋白质生产中产生稳定的变化，永久改变遗传的表达。表观遗传现象不仅在儿童的大脑中，而且在成人的大脑中，在调节神经功能方面发挥着至关重要的作用，因此环境对遗传负荷的作用和表达的影响在整个生命过程中都在不断发展[30]。表

观遗传模型为脆弱性的逐步构建提供了一个一般性的解释，脆弱性从发育早期暴露于有害的环境因素开始，通过这种暴露导致的基因表达的改变，并达到细胞生理学和有机体的功能，使抑郁症的发生发展风险增加。

3. 治疗及副作用

目前最常使用的一线抗抑郁药物：SSRI (五羟色胺重摄取抑制剂) [31]但其副作用则是一旦中断使用会使患者产生戒断反应，再则 NDRI (去甲肾上腺素&多巴胺重摄取抑制剂)和 SNRI (五羟色胺&去甲肾上腺素重抑制剂)也是一线常使用的药物[32]。二线药物包括：三环抗抑郁药、单胺氧化酶抑制剂，由于副作用太大药物疗法只有初期才改善，后期不受药物控制，可能是受体脱敏，也有可能是脑内新增了一些代偿机制[33]。如今刺激疗法也是新型抗抑郁的一种治疗手段包括：电休克刺激(ECT)经颅磁刺激(TMS)交感神经刺激(VNS)用脑电图与局部电刺激结合[34]，实现了适用于不同患者的个性化的刺激治疗效果差，其副作用则会给患者带来治疗痛苦。由于抑郁症的病因是再皮层和大脑内的边缘系统，这些地方的神经元主要释放谷氨酸和 GABA 这两种神经递质，氯胺酮是通过阻断外侧僵核的神经元放电，解除了对下游的单胺能奖赏通路的抑制，从而实现快速抗抑郁的疗效，目前还找到了氯胺酮在外侧僵核上的作用靶点，那就是表达在星形胶质细胞上的 Kir.4.1 通道[35]。

4. 中医药对抑郁症的认识

4.1. 中医抑郁的概念

抑郁症归属于传统医学的“郁证”“癫证”“百合病”“脏躁”“梅核气”等范畴。其病因病机是与气血、痰瘀及脏腑功能失常有关。气血失和，运行不畅，精液不能濡养脏腑，脏腑亏虚而为病[36]；“气血冲和，万病不生，一有怫郁，诸病生焉(《丹溪心法·六郁》)”，其以气机瘀滞为基础，气郁日久，血运不畅而致血瘀，郁而化火，上扰心神；情志刺激，肝失疏泄，肝郁气滞则气血运行受阻，神气失调；心主神明，情志内伤损伤心神，心气不足，心血不旺，心神不安；脾虚则心气不足，子病及母，脾居中央，土枢四象，五脏中皆有脾气，脾气郁则五脏气郁，最终使五脏之神魂魄意志皆无所主[37]；肺气郁结，治节失常，肺失宣降，一身之气机升降出入不利，津液输布障碍，郁而为病；肾者，五脏之根本，肾精亏虚，髓海不足，脑失所养，肝肾母子相生、肝肾精血互化、肝肾藏泻互用及肝肾同源于脑，气血，痰瘀、五脏相互影响，共同致使抑郁症出现[38]。

4.2. 中医药的治疗

中药复方治疗详见表 1：

Table 1. Traditional Chinese medicine compound therapy for depression
表 1. 中药复方治疗抑郁症

复方	功效	机制	参考文献
越鞠丸	解诸郁	上调抗抑郁活性的神经回路	[39]
栀子汤	清热退黄	减轻氧化应激损伤	[40]
开心散	安神、补气、利湿化浊	1) 抑制 BV2 细胞 TLR4/IKK/NF-κB 通路降低炎症因子的表达	[41]
		2) 抑制小鼠海马小胶质细胞的活化，调节促炎细胞因子的表达	[41]

Continued

柴胡疏肝散	疏肝理气，行气止痛	通过 PI3K/AKT 途径参与重性抑郁障碍(MDD)治疗	[42]
加味逍遥散	疏肝通络，化痰消肿	通过触发自噬体形成减轻神经元凋亡改善抑郁样行为	[43]
小柴胡汤	和解少阳	1) 通过 PI3K/AKT 途径参与重性抑郁障碍的治疗	[44]
		2) 调节肠道菌群	[45] [46]
枳壳厚朴汤	行气除胀、厚肠止痢	增加大鼠海马 CA1 中 5-羟色胺受体 1A (HTR1A)蛋白和 5-羟色胺受体 1A (HTR1A) mRNA 的表达	[47]
百合地黄汤	养阴清热，补益心肺	1) 通过调节海马神经元的突触可塑性来改善焦虑和抑郁行为	[48]
		2) 通过调节 miRNA-144-3p 介导的 GABA 合成和释放来改善生长抑素(SST)阳性神经元缺陷	[49]
二仙汤	补肾益精、养血安神	调节围绝经期抑郁小鼠的激素分泌，修复海马损伤	[50]
麻黄附子细辛汤	助阳解表	通过调节 NLRP3 炎症小体和神经发生逆转 LPS 诱导小鼠的抑郁样行为	[51]
柴胡加龙骨牡蛎汤	疏肝泄热，重镇安神	通过增强海马 BDNF 的表达而立即和持久地产生抗抑郁作用	[52]
交泰丸	调营和中、交通心肾	以调节氨基酸代谢、甘油磷脂代谢和能量代谢抗抑郁	[53]

中药单药治疗详见表 2：

Table 2. Traditional Chinese medicine monotherapy for depression
表 2. 中药单药治疗抑郁症

中药	药理作用	机制	参考文献
牛大力	润肺滋肾、平肝补虚、活血强精、通络止痛	调节 Maoa、Maob、Ache、Ido1 和 Comt 等 5 个靶点，以及色氨酸代谢、神经递质合成和磷脂代谢 3 条代谢途径来改善抑郁症	[54]
甘松	具有行气止痛，开郁醒脾	增强了 5-羟色胺转运体活性具有抗抑郁的作用	[55]
芍药	疏肝、柔肝、止痛	上调单胺类神经递质水平、抑制下丘脑－垂体－肾上腺轴功能亢进、促进神经保护、促进海马神经发生、促进神经再生、促进神经功能亢进等。以及上调脑源性神经营养因子水平、抑制炎症反应、下调一氧化氮水平	[56]
人参	大补元气，复脉固脱，补脾益肺，生津，安神	调节单胺类神经递质系统、上调神经营养因子的表达、调节 HPA 轴的功能和抗炎作用	[57]
香附	疏肝理气、调经止痛	其提取物 α-香附酮、罗通定苷 G 具有抗抑郁作用	[58]
苦参	清热燥湿、杀虫止痒	通过抗炎而抗抑郁	[59]
黄连	清热燥湿、泻火通便	通过抑制自噬和凋亡来保护 PC12 细胞免受氧化应激	[60]
萱草	清热、利尿、凉血、止血	通过调节 MAOA、MAOB 和 ESR1 来缓解抑郁症状	[61]

Continued

黄芩	清热燥湿、泻火解毒	通过上调 PGC-1α 抑制神经炎症	[62]
黄精	补气养阴，润肺，健脾，滋肾	通过减少 ROS/HPA 轴功能亢进和炎症反应来防止抑郁样行为和突触及神经元损伤	[63]
百合	养阴润燥、安心养神、健胃补脾	通过下调 MYC 减少抑郁样行为小鼠海马小胶质细胞的活化和凋亡	[64]
藏红花	活血化瘀、凉血解毒、解郁安神、美容养颜	通过抑制 NF-kB 和 NLRP3 信号通路减轻脂多糖诱导的焦虑和抑郁样行为	[65]
地黄	清热凉血，养阴生津	恢复 HPA 轴功能障碍，增强单胺能神经系统，上调 BDNF 和 TrkB 表达	[66]
钩藤	息风定惊、止抽	调节了神经递质和神经内分泌激素的水平	[67]
五味子	敛肺、滋肾、生津、收汗、涩精	通过调节与 GPR81 受体介导的脂质代谢途径相关的肠道微生物群衍生物来改善焦虑和抑郁样行为	[68]
菊花	疏散风热，平肝明目，清热解毒	通过干扰色氨酸代谢、精氨酸和脯氨酸代谢、柠檬酸循环、烟酸和烟酰胺代谢、苯丙氨酸代谢、丙氨酸、天冬氨酸和谷氨酸代谢发挥抗抑郁作用	[69]

中药提取物治疗详见表 3：

Table 3. Traditional Chinese medicine extracts for the treatment of depression
表 3. 中药提取物治疗抑郁症

中药化合物	来源	机制	参考文献
厚朴酚	厚朴	1) 通过调节糖皮质激素受体介导的负反馈机制和糖皮质激素与盐皮质激素受体之间的平衡来恢复下丘脑－垂体－肾上腺轴的活性	[70]
		2) 通过 NF-κB 信号通路抑制 LPS 诱导的神经炎症反应	[71]
芍药苷	芍药	通过抑制海马中小胶质细胞的激活	[72]
栀子油	栀子	有效地增强了海马区蛋白激酶(PKA)、环磷酸腺苷反应元件结合蛋白(p-CREB)和脑源性神经营养因子(BDNF)的表达，对抑郁症发挥保护作用	[73]
人参皂苷	人参	1) 抑制兴奋性毒性，调节神经生长因子，促进神经再生。而营养神经对抑郁症有预治作用	[74]
		2) 改善由海马中星形胶质细胞间隙连接功能障碍诱导的大鼠的抑郁样行为	[75]
		3) 通过 PPARγ 介导的小胶质细胞激活和促进成年海马神经发生来减轻 CMS 暴露雄性小鼠的抑郁样行为	[76]
淫羊藿苷	淫羊藿	调节了脑内神经递质地分泌，增强了免疫功能，调节 PI3K-AKT 通路相关蛋白的表达	[77]

Continued

巴戟天寡糖	巴戟天	通过抑制 NLRP3 炎症小体抑制海马炎症减轻抑郁样行为	[78]
仙茅苷	仙茅	增加海马 BDNF 促进恐惧消除和预防小鼠获得性无助模型中的抑郁样行为	[79]
绞股蓝皂甙	绞股蓝	抑制海马神经炎症逆转抑郁行为	[80]
柴胡皂苷 a	柴胡	通过恢复围绝经期海马的神经内分泌、神经炎症和神经营养系统而抗抑郁	[81]
黄芩苷	黄芩	1) 通过 Akt/FOXG1 途径促进神经元的分化，转化为成熟神经元并促进其存活	[82]
		2) 抑制抑郁模型大鼠 GSK3β/NF-κB/NLRP3 信号通路的激活发挥神经保护作用	[83]
		3) 激活 Rac1-cofilin 通路，并随后改善突触可塑性	[84]
甘草苷	甘草	通过抑制神经炎症和维持突触发生来增强 FGF-2，从而在 LPS 诱导的抑郁症中发挥抗抑郁样作用	[85]
姜黄素	姜黄	上调 GAS5 可以降低 miR-10b，从而影响 BDNF mRNA 水平	[86]
藏红花素	藏红花	抑制 NLRP3 炎症小体和 NF-κB 及其促进小胶质细胞的 M1 向 M2 表型转化	[87]
小檗碱	黄连	下调了应激状态下的血浆皮质醇和促肾上腺皮质激素水平，并上调了 BDNF 蛋白表达，保护神经元	[88]
芍药内酯苷	芍药	通过抑制海马胞质磷脂酶 A2 (cPLA2)使磷脂代谢中的代谢失调正常化；抑制 cPLA2 过度表达，通过 cPLA2 蛋白激酶 B (AK t1) - 吲哚胺 2,3-双加氧酶 1 (IDO1)调节环纠正色氨酸代谢的异常犬尿氨酸途径	[89]
反式肉桂醛	肉桂	提高小鼠海马 5-HT 水平，降低 Glu/GABA 比值。与 SAL + FST 组相比，TCA + FST 组显著降低小鼠海马 COX-2、TRPV1 和 CB1 蛋白水平($p < 0.05$, $p < 0.05$, $p < 0.01$)。这些发现表明，TCA 治疗发挥了抗抑郁作用，并能够调节 FST 中的神经递质	[90]
羟基红花黄色素 A	红花	抑制 HPA 信号传导、抑制海马炎症和氧化应激来改善抑郁行为	[91]
柴胡皂苷-d	柴胡	降低了与 LPS 刺激的 BV2 小胶质细胞共培养的 SH-SY5Y 细胞中 LPA1 的表达和神经元凋亡的程度	[92]
天麻素	天麻	抑制海马中 er 应激和 NLRP3 炎症体激活	[93]
女贞子酚苷	女贞子	抑制小鼠下丘脑中的神经炎症改善了 LPS 诱导的抑郁样行为	[94]
麝香酮	麝香	抑制小胶质细胞活化和炎性细胞因子的产生，从而抑制小鼠前额叶皮质的神经炎症	[95]
柴胡皂苷 A	柴胡	1 通过 p-CREB/BDNF 通路改善脑缺血后抑郁样行为并抑制海马神经元凋亡	[96]
川续断皂苷 VI	川续断	通过下调 IDO 的表达和使异常的谷氨酸传递正常化而具有抗抑郁作用	[97]

Continued

人参皂苷 Rb1	人参	通过 AKT 通路激活海马、血清和小胶质细胞的抗炎作用	[98]
管花肉苁蓉总苷	肉苁蓉	调节肠道微生物	[99]

5. 总结与展望

至若情志之郁，则总由乎心，此因郁而病也。则抑郁症可由病而郁，也可由郁而病，是一种复杂的身心疾病，不可简单地划分为心理疾病或者器质性疾病。当前对于抑郁症的治疗，一线临床用药多选用不同类型的西药，但存在疗效不佳，起效慢，副作用大等问题。中医药由于其辨证论治，根据患者的不同证型进行个性化诊断配药，且安全，副作用小等，易于被患者接受，故成为现代临床治疗抑郁症的一种重要手段。根据现有研究显示无论是单味药或者复方或者中药提取化合物，其抗抑郁的作用机理多涉及单胺类神经递质系统、神经炎症、神经可塑性以及神经营养等方面，中药治疗抑郁症是通过靶点、多成分来发挥作用虽然中医药联合治疗抑郁症有巨大的潜在优势，可也存在部分问题等待解决：1) 中医药治疗抑郁症是以辩证论治为基础，这就需要中医师有较高的医疗水平能够对每位患者准确辩证，而目前对于每个证型的标准并没有一个准确的规范，且各个医院医师水平不一；2) 中药方剂多成分，多靶点在治疗抑郁共病方面具有优势，但是目前抑郁症的发病机制没有明确解释，因此对于中药治疗抑郁症的药效也无法得到准确验证。中医药联合治疗抑郁症虽然有一定的可行性，但也存在着以上问题需要解决，还需要进行更深入的研究。

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