

英国中医药学会  
**The Association of Traditional Chinese Medicine and Acupuncture UK**

## TCM Research Updates

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# Wen Dan Decoction for hemorrhagic stroke and ischemic stroke

<http://www.ncbi.nlm.nih.gov/pubmed/25847568>

Complement Ther Med. 2015 Apr;23(2):298-308

BY Xu JH

## Abstract

### OBJECTIVE:

The use of traditional Chinese medicine (TCM) in stroke is increasing worldwide. Here we report the existing clinical evidence of the Pinellia Ternata containing formula Wen Dan Decoction (WDD) for the treatment of ischemic stroke and hemorrhagic stroke.

### METHODS:

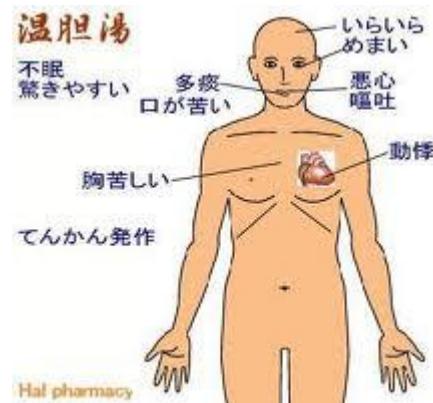
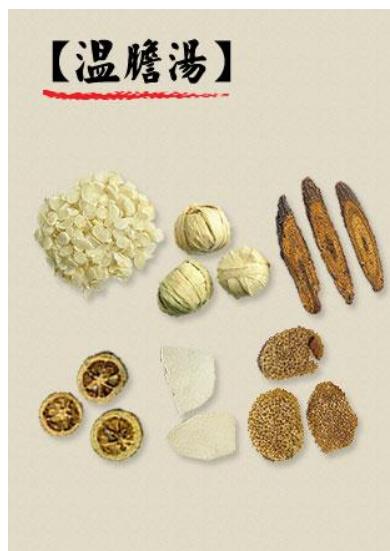
PubMed, CNKI, Wan Fang database, Cochrane Library and online Clinical Trial Registry were searched up to 26 February 2013 for randomized, controlled clinical trials (RCTs) using WDD as intervention versus Western conventional medicine as control to treat stroke. Clinical outcomes were improvement of the Neurological Functional Deficit Scores (NFDS) and overall therapeutic efficacy rates including rate of cure. Meta-regression analysis using Hedges'g was performed for RCTs with significant heterogeneity.

## RESULTS:

A total of 22 RCTs of ischemic stroke and 4 RCTs of hemorrhagic stroke, involving 2214 patients (1167 used WDD), met our inclusion criteria. Meta-analysis of the 13 RCTs reporting NFDS improvement favored WDD over the control (mean difference=-3.40, 95% confidence intervals [CI]=[-4.64, -2.15]). Rate of overall therapeutic efficacy (odds ratio [OR]=3.39, 95%CI=[1.81, 6.37]) for hemorrhagic stroke were significantly higher in WDD treated patients than the control subjects. In the 1898 patients with ischemic stroke, WDD medication also achieved higher rates of cure (OR=2.22, 95%CI=[1.66, 2.97]) and overall therapeutic efficacy (OR=3.31, 95%CI=[2.54, 4.31]) than the conventional treatment.

## CONCLUSIONS:

WDD displays benefits on improvement of neurological function and overall therapeutic efficacy in post-stroke patients. TCM such as WDD may serve as a therapeutic tool of dual actions to explore the common mechanisms underlying cerebral hemorrhage and ischemia.



# The traditional herbal medicine, Ge-Gen-Tang, inhibits pacemaker potentials by nitric oxide/cGMP dependent ATP-sensitive K(+) channels in cultured interstitial cells of Cajal from mouse small intestine.

<http://www.ncbi.nlm.nih.gov/pubmed/26003723>

J Ethnopharmacol. 2015 Jul 21;170:201-9

By Lee S

## Abstract

### ETHNOPHARMACOLOGICAL

#### RELEVANCE:

Ge-Gen-Tang (GGT) is a traditional Chinese medicinal formula composed of Puerariae radix (Pueraria lobata Ohwi), Ephedrae Herba (Ephedra sinica Stapf), Cinnamomi Ramulus (Cinnamomum cassia Blume), Paeoniae Radix (Paeonia lactiflora Pallas), Glycyrrhizae Radix preparata (Glycyrrhiza uralensis Fischer), Zingiberis Rhizoma (Zingiber officinale Roscoe), and Zizyphi Fructus (Ziziphus jujuba Mill. var. inermis Rehder) and is widely used to ameliorate the symptoms of gastrointestinal (GI) disorders related to diarrhea and intestinal mucosal immunity and for anti-cold, antipyretic and analgesic in Eastern Asia.

#### AIM OF THE STUDY:

Interstitial cells of Cajal (ICCs) are pacemaker cells in the GI tract that generate rhythmic oscillations in membrane potentials known as slow waves. We investigated the effects of GGT on pacemaker potentials in cultured ICCs from the mouse small intestine, and sought to identify the receptors and the action mechanisms involved.

#### MATERIALS AND METHODS:

Enzymatic digestions were used to dissociate ICCs from mouse small intestine tissues. All experiments on ICCs were performed on within

12h after culture. A whole-cell patch-clamp configuration was used to record potentials (current clamp) from cultured ICCs. Intracellular  $\text{Ca}^{2+}$  ( $[\text{Ca}^{2+}]_i$ ) increase was studied in cultured ICCs using fura-2AM. All of the experiments were performed at 30-32°C.

#### RESULTS:

Under the current clamping mode, GGT decreased the amplitude and frequency of pacemaker potentials; however, these effects were blocked by intracellular GDP $\beta$ S, a G-protein inhibitor, and glibenclamide, a specific ATP-sensitive K(+) channels blocker. Prazosin ( $\alpha$ 1-adrenoceptor antagonist) and butoxamine ( $\beta$ 2-adrenoceptor antagonist) did not block the GGT-induced effects, whereas atenolol ( $\beta$ 1-adrenoceptor antagonist) blocked the GGT-induced effects. Also, yohimbine ( $\alpha$ 2-adrenoceptor antagonist) partially blocked the GGT-induced effects. Pretreatment with SQ-22536, an adenylate cyclase inhibitor, did not block the GGT-induced effects, whereas pretreatment with ODQ, a guanylate cyclase inhibitor, or L-NAME, an inhibitor of nitric oxide (NO) synthase, did. Additionally,  $[\text{Ca}^{2+}]_i$  analysis showed that GGT decreased  $[\text{Ca}^{2+}]_i$ .

#### CONCLUSION:

These results suggest that GGT inhibits pacemaker potentials in ICCs in a G protein-, cGMP- and NO-dependent manner through stimulation of  $\alpha$ 2 and  $\beta$ 1-adrenoceptors.

# Metabolomic profiles illuminate the efficacy of Chinese herbal Da-Cheng-Qi decoction on acute pancreatitis in rats.

<http://www.ncbi.nlm.nih.gov/pubmed/26048200>

Pancreatology. 2015 May 11. pii: S1424-3903(15)

By Li J.

## Abstract

### BACKGROUND AND OBJECTIVES:

Chinese herbal drug Da-Cheng-Qi decoction (DCQD) has been widely used for decades to treat acute pancreatitis (AP). Previous trials are mostly designed to state the potential mechanisms of the therapeutic effects rather than to detect its whole effect on metabolism. This study aimed to investigate the efficacy of DCQD on metabolism in AP.

### METHODS:

Twenty-two male adult Sprague-Dawley rats were randomized into three groups. AP was induced by retrograde ductal infusion of 3.5% sodium taurocholate solution in DCQD and AP group, while 0.9% saline solution was used in sham operation (SO) group. Blood samples were obtained 12 h after drug administration and a 600 MHz superconducting Nuclear Magnetic Resonance (NMR) spectrometer was used to detected plasma metabolites. Principal Components Analysis (PCA) and Partial Least

Squares-Discriminant Analysis after Orthogonal Signal Correction (OSC-PLS-DA) were applied to analyze the Longitudinal Eddy-delay (LED) and Carr-Purcell-Meiboom-Gill (CPMG) spectra.

### RESULTS:

Differences in concentrations of metabolites among the three groups were detected by OSC-PLS-DA of  $^1\text{H}$ NMR spectra (both LED and CPMG). Compared with SO group, DCQD group had higher levels of plasma glycerol, glutamic acid, low density lipoprotein (LDL), saturated fatty acid (FA) and lower levels of alanine and glutamine, while the metabolic changes were reversed in the AP group.

### CONCLUSIONS:

Our results demonstrated that DCQD was capable of altering the changed concentrations of metabolites in rats with AP and  $^1\text{H}$ NMR-based metabolomic approach provided a new methodological cue for systematically investigating the efficacies and mechanisms of DCQD in treating AP.



# Immune-modulatory effects of bu-zhong-yi-qi-tang in ovalbumin-induced murine model of allergic asthma

<http://www.ncbi.nlm.nih.gov/pubmed/26035827>

PLoS One. 2015 Jun 2;10(6):e0127636

By Yang SH

## Abstract

### BACKGROUND:

Bu-zhong-yi-qi-tang (BZYQT), an herbal formula of traditional Chinese medicine, has been an effective regimen of allergic diseases for nearly 800 years. Our previous report has demonstrated its anti-inflammatory effects in patients with perennial allergic rhinitis, and the aim of this study is to investigate the anti-asthmatic effect of BZYQT.

### METHODS:

Female BALB/cByJNarl mice were sensitized with normal saline (control group) or OVA. Mice sensitized by OVA were fed with distilled water (OVA group), oral 0.5 g/Kg (low-dose group) or 1 g/Kg (high-dose group) of BZYQT solution once daily on days 36-40 besides their routine diet. Airway hyper-responsiveness (AHR), eosinophil infiltration, levels of cytokines and total immunoglobulin E (IgE) in broncho-alveolar lavage fluid (BALF) were determined. The lungs and tracheas were removed, and histopathologic examination was subsequently performed.

### RESULTS:

AHR was significantly reduced in both low- and high-dose BZYQT groups compared with the OVA group after inhalation of the highest dose of methacholine (50 mg/ml). The levels of eotaxin, Th2-related cytokines (IL-4, IL-5, IL-13), IgE, and eosinophil infiltration in BALF were significantly decreased in both BZYQT groups compared with the OVA group. Histopathologic examination revealed that eosinophil infiltration of the lung and trachea tissues was remarkably attenuated in both BZYQT groups.

### CONCLUSIONS:

Oral administration of BZYQT solution may exert anti-asthmatic effect by relieving AHR in OVA-sensitized mice, which is compatible with our clinical experience. Although detailed mechanism is to be determined, we surmise that it may be correlated with the immune-modulatory effects of inhibiting Th2 responses on the basis of our limited results.



# Berberine Sensitizes Human Ovarian Cancer Cells to Cisplatin Through miR-93/PTEN/Akt Signaling Pathway.

<http://www.ncbi.nlm.nih.gov/pubmed/26087719>

Cell Physiol Biochem. 2015 Jun 12;36(3):956-965.

By Chen Q

## Abstract

### BACKGROUND:

Berberine, a well-known component of the Chinese herbal medicine Huanglian, has wide range of biochemical and pharmacological effects, including antineoplastic effect, but the exact mechanisms remain unclear. The aim of the present study was to evaluate the potential chemo-sensitization effect of berberine in ovarian cancer cell line A2780.

### METHODS:

The expression of miR-93 was measured by RT-PCR. The target of miR-93 was confirmed by luciferase activity assay. Hoechst 33258 staining, Annexin V and PI double staining were used for apoptosis analysis.

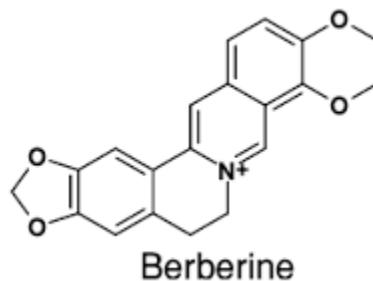
### RESULTS:

In this study, we found A2780/DDP cells that were incubated with berberine combined with cisplatin had a significantly lower survival than the control group. Berberine enhanced cisplatin

induced apoptosis and induced G0/G1 cell cycle arrest in A2780 cells. Next, we observed that the miR-93 levels in cisplatin resistant cell lines were higher than that in cisplatin sensitive cell lines. Furthermore, our study found berberine could inhibit miR-93 expression and function in ovarian cancer, as shown by an increase of its target PTEN, an important tumor suppressor in ovarian cancer. A2780 cells that were treated with PTEN siRNA had increased survival compared to NC group and this could be partly alleviated by the AKT inhibitor Triciribine. More importantly, A2780 cells that were treated with PTEN siRNA had a survival pattern that is similar to cells with miR-93 overexpression.

### CONCLUSION:

The results suggested that berberine modulated the sensitivity of cisplatin through miR-93/PTEN/AKT signaling pathway in the ovarian cancer cells.



# Combination Efficacy of Astragalus membranaceus and Curcuma wenyujin at Different Stages of Tumor Progression in an Imageable Orthotopic Nude Mouse Model of Metastatic Human Ovarian Cancer Expressing Red Fluorescent Protein.

<http://www.ncbi.nlm.nih.gov/pubmed/26026079>

Anticancer Res. 2015 Jun;35(6):3193-207

By Yin G

## Abstract

### **BACKGROUND/AIM:**

The present study determined the efficacy of extracts of Astragalus membranaceus (AM) and Curcuma wenyujin (CW), a traditional Chinese medicine herbal mixture, at different tumor stages of an orthotopic nude mouse model of human ovarian cancer expressing red fluorescent protein.

### **MATERIALS AND METHODS:**

The tumor-bearing mice were treated with cisplatin (CDDP), AM, CW, or a combination of AM and CW in each of three tumor stages, using the same regimen. Group 1 received saline as negative control. Group 2 received CDDP i.p. as positive control with a dose of 2 mg/kg, every three days. Group 3 received AM daily via oral gavage, at a dose of 9120 mg/kg. Group 4 received CW daily via oral gavage, at a dose of 4560 mg/kg. Groups 5, 6 and 7 received combinations of AM and CW daily via oral gavage at low (AM, 2280 mg/kg; CW, 1140 mg/kg), medium (AM, 4560 mg/kg; CW 2280 mg/kg), and high (AM, 9120 mg/kg; CW, 4560 mg/kg) doses. The expression of angiogenesis- and apoptosis-related genes in the tumors were analyzed by immunohistochemistry for matrix metalloproteinase 2 (MMP-2), vascular

endothelial growth factor (VEGF) fibroblast growth factor 2 (FGF-2), B-cell lymphoma 2 (Bcl-2) and cyclooxygenase 2 (Cox-2), and by polymerase chain reaction for MMP-2, FGF-2 and Bcl-2.

### **RESULTS:**

CDDP, AM, and its combination with CW-induced significant growth inhibition of Stage I tumors. Strong efficacy of the combination of AM and CW at high dose was observed. Monotherapy with CDDP, AM, CW, and the combination treatments did not significantly inhibit Stage II and III tumors. The expression of MMP-2, VEGF, FGF-2, and Cox-2 was significantly reduced in Stage I tumors treated with AM, CW, and their combination, suggesting a possible role of these angiogenesis- and apoptosis-related genes in the observed efficacy of the agents tested.

### **CONCLUSION:**

This study is the first report on the efficacy of anticancer agents at different stages of ovarian cancer in an orthotopic mouse model. As the tumor progressed, it became treatment-resistant, similar to the clinical situation, further demonstrating the utility of the model and the need for agents active in advanced-stage ovarian cancer.

# Yi Qi Qing Re Gao formula ameliorates puromycin aminonucleoside-induced nephrosis by suppressing inflammation and apoptosis.

<http://www.ncbi.nlm.nih.gov/pubmed/26014479>

BMC Complement Altern Med. 2015 May 27;15:155

By Wen Y

## Abstract

### BACKGROUND:

Yi Qi Qing Re Gao (YQQRG) formula is a traditional Chinese herbal medicine used to treat chronic nephritis. This study was designed to evaluate the underlying mechanism in the use of YQQRG formula to treat nephrosis induced by puromycin aminonucleoside (PAN).

### METHODS:

Thirty-six male Wistar rats were randomly divided into 3 groups of 12 rats each: a sham group, a vehicle-treated PAN model group(PAN), and a group treated with YQQRG (PAN + YQQRG). The PAN model was established by a single intravenous injection of PAN at a dose of 40 mg/kg body weight; rats in the sham group received the same volume of saline. Twenty-four hour urinary protein was measured 0, 3, 5, 10, and 15 days after the injection. The rats were sacrificed on day 10 and day 15 and the serum lipid profile examined. The renal cortex of each rat was stained with periodic acid-Schiff reagent and the pathologic alterations and ultrastructural changes were examined by transmission electron microscopy. In situ cell

apoptosis was detected by a terminal deoxynucleotidyl transferase-mediated uridine 5'-triphosphate-biotin nick end-labeling (TUNEL) assay. Transcriptive levels of inflammatory markers and molecules associated with apoptosis were detected by a real-time polymerase chain reaction and expression of proteins was examined by either immunohistochemistry or Western blot analysis.

### RESULTS:

YQQRG significantly decreased urinary protein level, and lowered serum lipid level. YQQRG also attenuated histologic lesions in the rat kidneys. Activation of inflammatory markers was largely restored by the administration of YQQRG. TUNEL assay showed that YQQRG decreased the number of apoptotic cells. Both mRNA and protein levels of caspase-3 were significantly reduced in the group treated with YQQRG, whereas expression of the Bcl-2 protein increased in the YQQRG group.

### CONCLUSIONS:

YQQRG alleviated kidney injury in PAN-treated rats, possibly through anti-inflammatory and anti-apoptotic effects.

# The potential utility of acetyl-tanshinone IIA in the treatment of HER2-overexpressed breast cancer: Induction of cancer cell death by targeting apoptotic and metabolic signaling pathways

<http://www.ncbi.nlm.nih.gov/pubmed/26068969>

Oncotarget. 2015 May 28.

By Guerram M

## Abstract

Increased lipogenesis and protein synthesis is a hallmark of cancer cell proliferation, survival, and metastatic progression and is under intense investigation as a potential antineoplastic target. Acetyl-tanshinone IIA (ATA) is a compound that was obtained from chemical modifications of tanshinone IIA (TIIA), a potent anticancer agent extracted from the dried roots of the Chinese herbal medicine *Salvia miltiorrhiza* Bunge. A previous investigation indicated that ATA is more effective in inhibiting the growth of breast cancer especially cells with HER2 overexpression. However, the molecular mechanism(s) mediating this cytotoxic effect on HER2-positive breast cancer remained undefined. Studies described here report that ATA induced G1/S phase arrest and apoptosis in the HER2-positive MDA-MB-453, SK-BR-3, and BT-474 breast cancer cell lines. Mechanistic

investigations revealed that the ATA-induced apoptosis effect is associated with remarkably down-regulation of receptor tyrosine kinases (RTKs) EGFR/HER2 and inhibition of their downstream pro-survival signaling pathways. Interestingly, ATA was found to trigger oxidative and endoplasmic reticulum (ER) stresses and to activate AMP activated protein kinase (AMPK) leading to inactivation of key enzymes involved in lipid and protein biogenesis. Intraperitoneal

administration of ATA significantly inhibited the growth of MDA-MB-453 xenografts in athymic mice without causing weight loss and any other side effects. Additionally, transwell migration, invasion, and wound healing assays revealed that ATA could suppress tumor angiogenesis in vitro. Taken together, our data suggest that ATA may have broad utility in the treatment of HER2-overexpressed breast cancers.

## Herbal traditional Chinese medicine and its evidence base in gastrointestinal disorders.

<http://www.ncbi.nlm.nih.gov/pubmed/25914456>

World J Gastroenterol. 2015 Apr 21;21(15):4466-4490

By Teschke R

## Abstract

Herbal traditional Chinese medicine (TCM) is used to treat several ailments, but its efficiency is poorly documented and hence debated, as opposed to modern medicine commonly providing effective therapies. The aim of this review article is to present a practical reference guide on the role of herbal TCM in managing gastrointestinal disorders, supported by systematic reviews and evidence based trials. A literature search using herbal TCM combined with terms for gastrointestinal disorders in PubMed and the Cochrane database identified publications of herbal TCM trials. Results were analyzed for study type, inclusion criteria, and

outcome parameters. Quality of placebo controlled, randomized, double-blind clinical trials was poor, mostly neglecting stringent evidence based diagnostic and therapeutic criteria. Accordingly, appropriate Cochrane reviews and meta-analyses were limited and failed to support valid, clinically relevant evidence based efficiency of herbal TCM in gastrointestinal diseases, including gastroesophageal reflux disease, gastric or duodenal ulcer, dyspepsia, irritable bowel syndrome, ulcerative colitis, and Crohn's disease. In conclusion, the use of herbal TCM to treat various diseases has an interesting philosophical background with a long history, but it received increasing skepticism due to the lack of evidence based efficiency as shown

by high quality trials; this has now been summarized for gastrointestinal disorders, with TCM not recommended for most gastrointestinal diseases. Future studies should focus on placebo controlled, randomized, double-blind clinical trials, herbal product quality and standard criteria for diagnosis, treatment, outcome, and

assessment of adverse herb reactions. This approach will provide figures of risk/benefit profiles that hopefully are positive for at least some treatment modalities of herbalTCM. Proponents of modern herbal TCM best face these promising challenges of pragmatic modern medicine by bridging the gap between the two medicinal cultures

## Cognitive Improvement during Treatment for Mild Alzheimer's Disease with a Chinese Herbal Formula: A Randomized Controlled Trial.

<http://www.ncbi.nlm.nih.gov/pubmed/26076022>  
PLoS One. 2015 Jun 15;10(6):e0130353

By Zhang Y.

### Abstract

#### **OBJECTIVES:**

To explore the efficacy of Chinese herbal formula compared with donepezil 5mg/day in patients with mild Alzheimer's disease (AD).

#### **METHODS:**

Patients with mild AD meeting the criteria were randomized into Chinese herbal formula Yishen Huazhuo decoction (YHD) group and donepezil hydrochloride (DH) group during the 24-week trial. The outcomes were measured by ADAS-cog, MMSE, ADL, and NPI with linear mixed-effect models.

#### **RESULTS:**

144 patients were randomized. The mean scores of ADAS-cog and MMSE in both

YHD group and DH group both improved at the end of the 24-week treatment period. The results also revealed that YHD was better at improving the mean scores of ADAS-cog and MMSE than DH. Linear mixed-effect models with repeated measures showed statistical significance in time × group interaction effect of ADAS-cog and also in time × groupinteraction effect of MMSE. The data showed YHD was superior to DH in improving the scores and long term efficacy.

#### **CONCLUSIONS:**

Our study suggests that Chinese herbal formula YHD is beneficial and effective for cognitive improvement in patients with mild AD and the mechanism might be through reducing amyloid- $\beta$  (A $\beta$ ) plaque deposition in the hippocampus.

## Herbal formula menoprogen alters insulin-like growth factor-1 and insulin-like growth factor binding protein-1 levels in the serum and ovaries of an aged female rat model of menopause

<http://www.ncbi.nlm.nih.gov/pubmed/26057826>

Menopause. 2015 Jun 8.

By Wei M

## Abstract

### OBJECTIVE:

Menoprogen (MPG), a traditional Chinese medicine formula for menopause, improves menopausal symptoms; however, its mechanism remains unknown. Previous studies have shown that MPG is not directly estrogenic; thus, the goal of this study was to investigate the effects of MPG on insulin-like growth factor-1 (IGF-1) and insulin-like growth factor binding protein-1 (IGFBP-1) levels in an aged female rat model of menopause.

### METHODS:

In a six-arm study, 14-month-old female Sprague-Dawley rats ( $n = 8$  per arm) were randomly divided into the following groups: untreated aged,  $17\beta$ -estradiol-treated aged

(estradiol [E2]), and three arms with increasing doses of MPG (162, 324, or 648 mg/kg/d). The sixth arm contained 4-month-old female Sprague-Dawley rats as a normal comparison group. Four

weeks after MPG or E2 administration, animals were killed after blood draws, and ovarian tissues were excised. Levels of E2 and progesterone (P4) were determined by radioimmunoassay. Serum and ovarian tissue levels of IGF-1, IGFBP-1, and IGF-1 receptor were determined by enzyme-linked immunosorbent assay.

### RESULTS:

Compared with the normal group, aged rats had significantly reduced serum levels of E2, P4, and IGF-1, and increased serum and ovarian tissue levels of IGFBP-1. MPG restored serum IGF-1 and IGFBP-1 levels and down-regulated ovarian levels of IGFBP-1, which were closely related to increases in E2 and P4 levels in aged rats. No significant differences in either IGF-1 or IGFBP-1 were observed between the three doses of MPG.

### CONCLUSIONS:

MPG exerts a direct in vivo effect on aged female rats by positively regulating serum and ovarian IGF-1 and IGFBP-1 levels.