Research No. 1

Title: The possible protective effect of simvastatin and pioglitazone separately and in combination on bleomycin-induced changes in mice thin skin.

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Tissue and Cell (January 2015). 47: 159-170

Abstract:

Bleomycin is a chemotherapeutic agent with side effects especially on skin. Simvastatin is a cholesterol lowering drug with immunomodulatory, anti-inflammatory, and antifibrotic effects. Pioglitazone is a peroxisome proliferator-activated receptor- antidiabetic agent with antiproliferative effects on smooth muscle cells (SMCs), and antioxidant and anti-inflammatory actions. The aim of this study was to investigate the anti-inflammatory and antifibrotic efficiencies of simvastatin and pioglitazone separately and in combination against bleomycin-induced changes in mice thin skin using histological, immunohistochemical, and biochemical techniques. In this study, the mice were divided into seven groups, with each group undergoing treatment for 3 weeks: the control group, group 1 was administered 100 μl of bleomycin, group 2 was administered simvastatin (5 mg/kg/day), group 3 received pioglitazone (10 mg/kg/day), group 4 received simvastatin (5 mg/kg/day) 1 h before bleomycin, group 5 received pioglitazone (10 mg/kg/day) 1 h before bleomycin, and group 6 was administered simvastatin (5 mg/kg/day) and pioglitazone (10 mg/kg/day) 1 h before bleomycin. In group 2, dermal thickening, subcutaneous fat atrophy, degeneration of hair follicles, and thickening of cutaneous vessel walls were observed in addition to a significant increase in caspase-3 reaction, transforming growth factor beta 1 (TGF-1) expression, and hydroxyproline content. A reversal of the previous findings was markedly observed in group 6 compared with groups 4 and 5. We conclude that the concurrent administration of pioglitazone and simvastatin enhanced their beneficial effects in the reversal of bleomycin-induced changes in mice thin skin.

Research No. 2

Title: Effect of metformin and adriamycin on transplantable tumor model

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Tissue and Cell (July 2015). 47: 498–505.

Abstract:

Adriamycin is a cytotoxic anthracycline antibiotic used in treatment of many types of cancer. Metformin is antidiabetic drug and is under investigation for treatment of cancer. The aim of this work was to study the effect of each of adriamycin and metformin alone and in combination on solid Ehrlich carcinoma (SEC) in mice. Eighty BALB/C mice were divided into four equal groups: SEC group، SEC + adriamycin, SEC + metformin, SEC + adriamycin + metformin. Tumor volume, survival rate, tissue catalase, tissue reduced glutathione, tissue malondialdehyde, tissue sphingosine kinase 1 activity, tissue caspase 3 activity and tissue tumor necrosis factor alpha were determined. A part of the tumor was examined for histopathological and immunohistochemical study. Adriamycin or metformin alone or in combination induced significant increase in the survival rate, tissue catalase, reduced glutathione and tissue caspase 3 activity with significant decrease in tumor volume, tissue malondialdehyde, tissue sphingosine kinase 1 activity and tumor necrosis factor alpha and alleviated the histopathological changes with significant increase in Trp53 expression and apoptotic index compared to SEC group. In conclusion، the combination of adriamycin and metformin had a better effect than each of these drugs alone against transplantable tumor model in mice.

Research No. 3

Title: Garlic oil inhibits dextran sodium sulfate-induced ulcerative colitis in rats

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Life Sciences (January 2016). 146: 40-51

Abstract:

Aims: Garlic oil (GO) is used for centuries in folk medicine as a therapy for many diseases including inflammatory disorders. Recently, it has exhibited potent anti-oxidant, anti-inflammatory and immunomodulatory effects. Consequently, we evaluated the possible protective effect of GO in a rat model of colitis, induced by dextran sulfate sodium (DSS). Main methods: Colitis induced by allowing rats a free access to drinking water containing 5% DSS for 7 days, from day 1 to day 7. GO was administered orally in doses of 25, 50 and 100 mg/kg/day. Mesalazine used as a standard medication in a dose of 15 mg/kg/day. All animals fasted for 2 h, 1 h before and 1 h after giving the treatment, which introduced daily for 7 days, from day 1 to day 7, at 10:00 to 11:00 A.M. Animal body, and colonic weights, colonic myeloperoxidase (MPO), and superoxide dismutase (SOD) activities, colonic reduced-glutathione (GSH), malondialdehyde (MDA), tumor necrosis factor-α (TNF-α), interleukin (IL)-1β, and IL-10 levels, macroscopic and microscopic changes of colonic tissues were evaluated. Key findings: GO treatment significantly suppressed the elevated colonic weight, MPO activity, MDA, TNF-α and IL-1β levels. However, it potentiated the decrease body weight, colonic SOD activity, GSH and IL-10 levels. Moreover, it ameliorated the marked macroscopic and microscopic changes of colonic mucosa in a dose dependent manner. Significance: Garlic oil inhibits DSS-induced colitis in rats may be through its anti-oxidant, anti-inflammatory and immunomodulatory properties. Therefore, GO could be a promising protective agent recommended for UC patients.

Research No. 4

Title: Carvedilol suppresses circulating and hepatic IL-6 responsible for hepatocarcinogenesis of chronically damaged liver in rats

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Published in:
Toxicology and Applied Pharmacology (October 2016). 311:1-11

Abstract:
Carvedilol is an anti-oxidant non-selective β-blocker used for reduction of portal blood pressure, prophylaxis of esophageal varices development and bleeding in chronic liver diseases. Recently, it exhibited potent anti-inflammatory, anti-fibrotic, anti-proliferative and anti-carcinogenic effects. In the present study, we evaluated the possible suppressive effect of carvedilol on circulating and hepatic IL-6 levels responsible for hepatocarcinogenesis in a rat model of hepatic cirrhosis. Besides, its effect on hepatic STAT-3 levels, function tests, oxidative stress markers, and hydroxyproline content, hepatic tissue histopathological changes and immunohistochemical expression of E & N-cadherin. Nine-week-old male Wistar rats injected intraperitoneal by 1 ml/kg 10% CCL4 in olive oil three times/week (every other day) for 12 weeks to induce hepatic cirrhosis. Carvedilol (10 mg/kg/day suspended in 0.5% CMC orally), silymarin (50 mg/kg/day suspended in 0.5% CMC orally) or combination of both used to treat hepatic cirrhosis from 15th to 84th day. Our data showed that carvedilol and silymarin co-treatment each alone or in combination efficiently reduced the elevated serum IL-6, ALT, AST, ALP and BIL, hepatic IL-6, STAT-3, MDA levels and hydroxyproline content. In addition, it elevated the reduced serum ALB level, hepatic CAT activity and GSH level. Meanwhile, it apparently restored the normal hepatic architecture, collagen distribution and immunohistochemical E & N-cadherin expression. Furthermore, carvedilol was superior to silymarin in improving MDA level. Moreover, the combination of carvedilol and silymarin showed an upper hand in amelioration of the CCL4 induced hepatotoxicity than each alone. Therefore, carvedilol could be promising in prevention of hepatocarcinogenesis in chronic hepatic injuries.

Research No. 5

Title: Phloretin either alone or in combination with duloxetine alleviates the STZ induced diabetic neuropathy in rats

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Biomedicine & Pharmacotherapy (March 2018). 101: 821-832

Abstract:

Diabetic neuropathy (DN) is one of most disabling disorder complicating diabetes mellitus (DM), which affects more than 50% of the all diabetic patients during the disease course. Duloxetine (DX) is one of the first-line medication that approved by FDA for management of DN, nevertheless, it is too costly and has many adverse effects. Recently, phloretin (PH) exhibited powerful euglycemic, antihyperlipidemic, antioxidant, and anti-inflammatory activities. Therefore, we investigated the in vivo possible antineuropathic activity of phloretin, besides, its modulating effects on duloxetine potency, in a rat model of DN. Twelve-week-old male Wistar rats received a single intraperitoneal injection of 55 mg/kg STZ to induce DM. Either DX (30 or 15 mg/kg dissolved in distilled water), PH (50 0r 25 mg/kg dissolved in 0.5% DMSO) or a combination of 15 mg/kg DX and 25 mg/kg PH, used daily orally for 4 weeks to treat DN, starting from the end of the 4th week of DM development, when DN confirmed. Our finding showed that both DX and PH dose-dependently improved behavioral parameters (with the superiority of DX), sciatic nerve tissue antioxidant state, and suppressed tissue inflammatory cytokine, besides, they abrogated the tissue histopathological changes (with the superiority of PH). Moreover, DX augmented the DM metabolic disturbance and hepatic dysfunction, however, PH effectively amended these disorders. Furthermore, the low-dose combination of both, had the merits of both medications, with the alleviation of their disadvantages. Therefore, phloretin could be a promising agent in the management of DN either alone or in combination with duloxetine.

Research No. 6:

Title: Filgrastim (G-CSF) ameliorates Parkinsonism L-dopa therapy's drawbacks in mice

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Basal Ganglia (June 2018). 13: 17–26

Abstract:
L-dopa is still the cornerstone symptomatic medication for Parkinson disease (PD), although it cannot stop the neurodegenerative process progression or even aggravate it. Filgrastim (G-CSF) is a hematopoietic growth factor، exhibited neurotrophic, antioxidant, anti-apoptotic, immunomodulating and neuroprotective potentialities. The present study assessed the possible modulating potentialities of filgrastim on L-dopa treatment's drawbacks in a mouse model of PD. Male BALB/c mice received 30 mg/kg/day rotenone suspended in 0.25 ml 0.5% CMC in PBS for 28 days orally from day 1st until the day 28th of the experiment for induction of PD. Since day 29th till day 43rd, mice treated with either 10 mg/kg/day L-dopa and 2.5 mg/kg/day carbidopa suspended in 0.25 ml 0.5% CMC in PBS orally, 50 μg/kg/day filgrastim in 0.1 ml 5% dextrose SC or a combination of both. Filgrastim, in the present study, able to alleviate the L-dopa therapy's drawbacks in PD that revealed by the restoration of the exhausted nigrostriatal GSH level, and the reduction of the elevated nigrostriatal MDA, NO and TNF-α levels that deteriorated by L-dopa therapy. Moreover, the co-therapy of filgrastim with L-dopa, considerably potentiated the deteriorated mice's working memory, and abrogated the nigrostriatal histopathological changes and caspase-3 immunohistochemical expression, failed to improve by L-dopa therapy. Furthermore, the filgrastim co-therapy with L-dopa demonstrated a remarkable improvement in the nigrostriatal dopamine level, and repression of rotenone-induced descent latency prolongation, as well as, stride length reduction than each alone. Therefore، filgrastim is promising, as a disease-modifying therapy, in amelioration of L-dopa therapy's drawbacks in PD.

Research No. 7

Title: Apigenin and baicalin, each alone or in low-dose combination, attenuated chloroquine induced male infertility in adult rats

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Published in:
Thai Journal of Pharmaceutical Sciences (June 2018). 42(3): 1-11

Abstract:
Introduction: Male infertility is a worldwide health problem, which accounts for about 50% of all cases of infertility and considered as the most common single defined cause of infertility. Recently، apigenin and baicalin exhibited a powerful antioxidant and antiapoptotic activities. Consequently, in the present study, we evaluated the possible protective effect of apigenin and baicalin, either alone or in low-dose combination, on a rat model of male infertility, regarding for its effects on the hormonal assay, testicular weight, sperm parameters, oxidative-stress state, apoptosis, and histopathological changes. Material and methods: 12-week-old adult male Wister rats received 10 mg/kg/d chloroquine orally for 30 days to induce male infertility. Either apigenin (30 or 15 mg/kg/d), baicalin (100 or 50 mg/kg/d) or a combination of 15 mg/kg/d apigenin and 50 mg/kg/d baicalin received daily orally 1 h after chloroquine for 30 days, used to protect against chloroquine induced male infertility. Results and conclusion: Our result showed that both apigenin and baicalin, significantly and dose-dependently enhanced the reduced levels of serum testosterone، follicular stimulating, and luteinizing hormones (LHs), testicular weight, reduced-glutathione (GSH) level, and catalase (CAT) activity, sperm count, mobility, and viability, and suppressed the elevated testicular malondialdehyde (MDA) level, and caspase-3 immunohistochemical expression, as well as they, abrogated the disturbed testicular histopathological pictures, induced by chloroquine, with superiority of baicalin. Furthermore, the low-dose combination therapy was as effective as the high dose apigenin therapy, except for sperm viability, where it was as powerful as the baicalin high dose. Therefore, both apigenin and baicalin either alone or in low-dose combination could be promising in the management of male infertility.

Research No. 8:

Title: Olopatadine enhances recovery of alkali-induced corneal injury in rats

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Life Sciences (July 2018). 207: 499–507

Abstract:

Aims: The alkali-induced corneal injury is an ocular emergency that required an immediate and effective management to preserve the normal corneal functions and transparency. Olopatadine is a fast, topically-effective anti-allergic drug, which exhibited potent anti-inflammatory and anti-angiogenic abilities in different allergic animals' models. Therefore, this study aimed to evaluate the therapeutic effect of olopatadine on alkali-induced corneal injury in rats.

Materials and methods: Corneal alkali injury (CI) induced in the right eyes of an eight-week-old male Wister rats، by application of 3 mm diameter filter-papers, soaked for 10 s in 1 N-NaOH, to the right eyes' corneal centers for 30 s, afterward, the filter paper removed, and the rat right eye rinsed with 20 ml normal saline. For treatment of CI, either 0.2% or 0.77% olopatadine applied topically daily for 14 days, starting immediately after the induction of CI.

Key findings: Olopatadine, in the present work, effectively and dose-dependently enhanced the corneal healing after alkali application, with significant reduction of the corneal opacity and neovascularization scores, besides، it suppressed the augmented corneal IL-1β, VEGF, caspase-3 levels, and nuclear NF-κB immunohistochemical expression, meanwhile it abrogated the corneal histopathological changes, induced by alkali application.

Significance: Olopatadine appears to be a potential treatment option for alkali-induced corneal injury.