

## Investigation in Rats of the Antihyperglycaemic Effect of Plant Extracts Used in Taiwan for the Treatment of Diabetes Mellitus

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### ABSTRACT

In order to clarify the hypoglycaemic activity of plants that are widely used to diabetes mellitus in Taiwan, the present study investigated the effectiveness of ten plant extracts by screening the decrease of blood glucose level in streptozocin-induced diabetic rats. We found that only six plant extracts exhibited blood glucose lowering activities in the rat. Blood levels of insulin were also determined using radioimmunoassay methods. Lack of an increase of insulin-like immunoreactivity in rats treated with these six plant extracts ruled out the mediation of insulin-dependent mechanisms. Similar effects were also observed in glucose-challenged rats treated with these extracts. The results confirmed the hypoglycaemic activity of these plants and suggested that this action was produced through an insulin-independent mechanism.

**Key words:** blood glucose; streptozocin; diabetic rats; insulin; hypoglycaemic plants; Taiwan.

## **Inhibition of Platelet Activation and Endothelial Cell Injury by Polyphenolic Compounds Isolated from *Lonicera japonica* Thunb**

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### **ABSTRACT**

Effects of the polyphenolic compounds isolated from *Lonicera japonica* Thunb on platelet aggregation, platelet thromboxane biosynthesis and hydrogen peroxide-induced endothelial cell injury were studied. With regard to the inhibitory effect on human platelet aggregation, methyl caffeate, 3,4-di-O-caffeoylquinic acid and methyl 3,4-di-O-caffeoylquinic acid had a strong effect. They significantly inhibited the second wave of platelet aggregation induced by ADP. Concerning thromboxane biosynthesis triggered by calcium ionophore A23187 in platelets, methyl caffeate and methyl 3,4-di-O-caffeoylquinic acid had the most potent inhibitory effect. Methyl 3,4-di-O-caffeoylquinic acid directly inhibited the conversion of arachidonic acid to thromboxane by platelet microsomes, while methyl caffeate did not have any significant effect on thromboxane biosynthesis in platelet microsomes. In the prevention of hydrogen peroxide-induced endothelial cell injury in culture, protocatechuic acid, methyl caffeate, methyl chlorogenic acid and luteolin were significantly effective. The inhibitory effect on platelet activation and the cytoprotective effect on hydrogen peroxide-induced cell injury may explain the possible role of polyphenolic compounds isolated from *Lonicera japonica* Thunb in maintaining vascular homeostasis.

## Two Gallates from *Quercus glauca*

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### ABSTRACT

Two novel phenol glucoside gallates, querglanin and isoquerglanin, were isolated from the leaves of *Quercus glauca*. From chemical and spectroscopic evidence, they were characterized as 2-iso-propyl-4-hydroxyl-5-methyl phenol 1-O- $\beta$ -D-(6'-O-galloyl) glucopyranoside and 2-iso-propyl-4-hydroxyl-5-methyl phenol 1-O- $\beta$ -D-(3'-O-galloyl) glucopyranoside, respectively. In addition, the occurrence of seven known flavonoids was demonstrated.

**Key word Index-***Quercus glauca*; Fagaceae; phenol glycoside gallates; 2-iso-propyl-4-hydroxyl-5-methyl phenol 1-O- $\beta$ -D-(6'-galloyl) glucopyranoside; 2-iso-propyl-4-hydroxyl-5-methyl phenol 1-O- $\beta$ -(3'-O-galloyl) glucopyranoside; querglanin; isoquerglanin.

## **In vitro screening of antimotility effect on human sperm with polyphenolic compounds purified from Chinese herbal medicines**

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### **ABSTRACT**

Twenty-four kinds of pure compounds extracted from Chinese herbal medicines were studied for their effects on the human sperm motility. Seven of them were found to inhibit sperm motility at the concentration of 2 mg/ml. These 7 substances were further investigated for their sperm motility-inhibitory effect at the concentration of 3.0 mg/ml, 4.5 mg/ml, 6.75 mg/ml to test the dose-related response. The results showed that 5 of the 7 extracts, namely casuarinin, cinnamtannin B-1, pedunculagin, epicatechin-(4 $\beta$ -8)-epicatechin-(4 $\beta$ -8)-catechin and catechin have strong inhibitory effect on sperm motility with dose-response relationship. Since the chemical structures of these extracts have already been determined, further studies should aim to explore the mechanisms of their antimotility effect on human sperm. It would appear that some traditional chinese herbal medicine have the potential of becoming new and acceptable forms of male oral contraceptives in the future.

## Phenolics from *Kadsura japonica*

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### ABSTRACT

In addition to protocatechuic acid, gallic acid, (+)-catechin, (+)-gallocatechin, taxifolin, ampelopsin and rutin, two hydrolysable tannins, geraniin and chebulinic acid, were isolated from the fresh bark of *Kadsura japonica* (Schisandraceae). Their structures were established on the basis of spectroscopic evidence in conjunction with chemical reaction.

**Key words:** *Kadsura japonica*, Schisandraceae, phenolic acid, flavan-3-ol, flavonoid, hydrolysable tannin.

# **Tannins of Euphorbiaceous Plants. X. Antidesmin A, a New Dimeric Hydrolyzable Tannin from *Antidesma pentandrum* var. *barbatum***

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## **ABSTRACT**

A new hydrolyzable tannin antidesmin A (4), was isolated along with carpinusin (1) and geraniin (2) from dried leaves of *Antidesma pentandrum* Merr. var. *barbatum* Merr., and its dimeric structure, composed of davidiin (3) and geraniin (2) has been elucidated by spectral and Chemical methods.

# **Induction of Differentiation of the Human Promyelocytic Cekll Line (HL-60) by Conditioned Medium of Ceathea letifera-Stimulated Mononuclear Cells**

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## **ABSTRACT**

Studies by some investigators have shown that human leukemic cell lines, primarily of myeloid lineage, retain their ability to differentiate in vitro when exposed to a variety of compounds such as differentiation-inducing factors present in conditioned medium (CM) including retinoic acid [1], phorbol diesters [2], dimethyl sulfoxide, Clerodendron fragrans [3], and when cocultured in CMs secreted from lectin-stimulated lymphocytes or Chinese herb-stimulated mononuclear cells [4]. Recently, it became apparent from other studies that interferon- $\gamma$  (IFN- $\gamma$ ), colony-stimulating factor (CSF), and interleukin-2 (IL-2) have been identified in CM and have been found to express some of their effects by inducing differentiation. However, there is also an unidentified differentiation-inducing activity (DIA) distinct from the above well-known factors that has a similar effect [4].

There are only a few papers reporting CM of Chinese herb-stimulated mononuclear cells to have a capacity to induce differentiation of HL-60 cells. In the present study, we report another CM, called CL-CM, secreted from Ceathea letifera-stimulated mononuclear cells, which has the capacity to induce HL-60 cells to differentiate into mature cells.

## **Study of the Activities of Chinese Herb *Viscum alniformosanae* Part II: the Components of Conditioned Medium Produced by *Viscum alniformosanae*-Stimulated Mononuclear**

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### **ABSTRACT**

The human promyelocytic cell line HL-60 can be induced to monocytoïd terminal differentiation by several conditioned media produced by lectin-stimulated mononuclear cells. We reported previously that a 572-conditioned medium (CM) secreted from *viscum alniformosanae*-stimulated mononuclear cells also had the capacity of inducing HL-60 leukemic cells into mature monocytes. In the present study, we showed that 572-CM did not contain INF-r, TNF, IL-1 and IL-2 as determined by using ELISA tests. This CM was unable to induce granulocyte-macropage colony formation. Sodium dodecyl sulphate polyacrylamide gel electroporesis (SDS-PAGE) was used to detect the components of this CM. After running the acrylamide gels, a wide band protein, in the 65-80 kd range was obtained and it was different from those of other mitogens.



## **Review: Therapeutic Efficacy of Mebendazole, Praziquantel, Albendazole and Niclosamide for the Treatment of Taiwan Tenia Infection**

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### **ABSTRACT**

Taeniasis is an important public health problem among the aborigines in Taiwan. We have conducted intermittent but extensive field surveys of taeniasis among aborigines in the past seven years. Following the surveys, we have also used six taenicides (mixture of areca nuts and pumpkin seeds, atabrine, mebendazole, niclosamide, albendazole, and praziquantel) to treat thousands of aboriginal patients. Among these six taenicides praziquantel was shown to be the most effective, followed by atabrine and niclosamide, Albendazole is only slightly effective and mebendazole was not effective. Although areca nuts and pumpkin seeds mixture is highly effective against Taiwan Taenia, we do not recommend to use this drug for mass treatment because of its inconvenience. In addition to the evaluation of these drugs, a review of the chemotherapy of taeniasis in Taiwan was also presented in this paper.

## Studies on Taeniasis in Taiwan

### XV. Prevalence of Taeniasis in Paiwan, Rukai and Tsau Tribes of Aborigines in South Taiwan

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#### ABSTRACT

In order to understand the prevalence of taeniasis in Tsau, Paiwan, and Rukai aborigines, 366 Tsau school children in seven villages of Alishan District, Chiayi County were examined by a single scotch tape perianal swab and 488 Tsau adults in Laichi of the same district surveyed by the combined methods of questionnaire and showing gravid segments. The formalin-ether concentration method was used to examine 262 Paiwan adults in three villages of Taiwu District, Pingtung County, and 225 Rukai adults in three villages of Taiwu District, Kaohsiung County. The overall infection rates in the Tsau school children, Tsau, Paiwan, and Rukai adults were 0.5%, 0.02%, 3.8%, and 2.7%, respectively. After treatment with atabrine, each of one Tsau male and four Paiwan males expelled one Taiwan *Taenia* with scolex. The efficacy of this drug against taeniasis was 100%. At the same time, the local names of *Ascaris* and *Taenia* were also surveyed.

## Studies of Taeniasis in Taiwan

### XIV. Current Status of Taeniasis Among Yami Aborigines on Lanyu Island, Taitung County, Southeast Taiwan

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#### ABSTRACT

In December 1989, 1,457 Yami aborigines in six villages on Lanyu District (Lanyu Island), Taitung County, Southeast Taiwan, were examined by questionnaire and demonstration of the proglottides or by scotch tape perianal swab technique for taeniasis. The overall infection rate was 5%. The highest rate was found at Yehyin (8%) and the lowest at Yujen (2%). However, the rate did not significantly differ among the villages. The infection rate peaked in the 51-60 yr age group (15%) and the lowest rate was observed in the 11-20 yr age group (<1%). No infection was found in the 21-30 yr age group. The infection rates of men and women were similar (5%). Twenty-one per cent of 304 families was found to include one or more infected members and a family with five infected person was observed at Yehyin. The infection rate of taeniasis on Lanyu Island decreased from 16% in 1984 to 5% in 1989. However, 51 persons who were negative in 1984 were positive at present, 26 were found to be positive in both studies, and 216 (12 died) who were positive in 1984 were now negative. These results indicate that the Yami people still eat raw meat and viscera of animals.

**Key words:** taeniasis, Yami aborigine, Lanyu Island.

## Clinical manifestations of taeniasis in Taiwan aborigines

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### ABSTRACT

From 1974 to 1989, a total of 24,500 aborigines at 67 villages in ten mountainous districts/towns in Taiwan were examined for the Taiwan *Taenia* infection and 12% were found to be infected. In order to define the clinical manifestations of taeniasis caused by the Taiwan *Taenia*, 1661 aborigines in ten mountainous districts were surveyed. The overall clinical rate was 76%. The clinical rate was highest among Atayal aborigines (81%), followed by Bunun (66%) and Yami (61%) aborigines and lowest among Ami aborigines (40%). Among 1153 infected people, 10% had passed gravid segments in the faeces for less than 1 year, 24% for 1-3 years, 17% for 4-5 years, 23% for 6-10 years, 16% for 11-20 years, 7% 21-30 years, and 3% over 30 years. Twenty-six occurrences of gastrointestinal and neurological symptoms were reported by 1258 infected persons. Passing proglottides in the faeces (95%) was the most frequent sign, followed by pruritis ani (77%), nausea (46%), abdominal pain (45%), dizziness (42%), increased appetite (30%), headache (26%), ect.

**Key words:** *Taenia*, man, Taiwan, symptoms, Cestoda

## Experimental Infection of Philippine *Taenia* in Domestic Animals

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### ABSTRACT

In the present study, six 34-44-day-old Small-Ear-Miniature pigs and one 14-day-old Holstein calf were each fed 10,000 Philippine *Taenia* eggs and sacrificed 27-43 days after inoculation. The infection rate was 100% for both pigs and calf with cysticerci recovery rates of 11 and 6%, respectively. A total of 6431 cysticerci were recovered only from the livers of the six pigs and 597 only from the liver of the calf; more occurred in the parenchyma (pigs 75%, calf 83%) than on the surface (pigs 25%, calf 17%). Mature cysticerci were found in four of the six pigs. A total of 317 cysticerci recovered from the pig livers were mature and the rest were either immature (926), degenerate or calcified (5188). All 597 cysticerci recovered from the liver of the calf were degenerate or calcified. Measurements of length, width, diameter of protoscolex, rostellum, and sucker and hooklet pattern indicated that Philippine *Taenia* is very similar to *Taenia* from Taiwan, Korea, Indonesia and Thailand and very different from classical *T. saginata* and *T. solium*.

**Key words:** *Cysticercus*; rostellum; rudimentary rostellar hooklet; *Taenia*.

## The Study on the Complexation of Pertechnetate with Cysteine by Thin Layer Chromatography

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### ABSTRACT

The labelling of cysteine with  $^{99}\text{TcO}_4^-$  and  $^{99\text{m}}\text{TcO}_4^-$  in different cysteine concentration, reductant and pH value was studied by thin layer chromatography in this report. In the present of stannous chloride and cysteine the pertechnetate was firstly reduced to its lower oxidation state and complexed with cysteine. The yellow complex ( $\lambda_{\text{max}}=420\text{ nm}$ ) was formed in the initial stage and then gradually changed to the red one ( $\lambda_{\text{max}}=540\text{ nm}$ ) and green one ( $\lambda_{\text{max}}=645\text{ nm}$ ) during the reaction proceeding. Both of the complexation rate and the labelling yield increased with increasing of cysteine concentration at constant reductant concentration and pH values. The stannous chloride, pertechnetate, pH value and the reaction time not only majority factors to effect the labelling yield also effect the complex species. The pentavalent technetium complex (yellow) is the dominant species in the lower cysteine concentration (especially at 22.4 mM). When the cysteine concentration is higher enough or the reaction time is longer, the quadrivalent technetium complexes (red and green) become more preponderant. The label yield was calculated by double strip method, it was higher than 99% in the condition of 400 mM cysteine, 7.5 mM stannous chloride and 12.5 mM peretech-nate at pH 8 within 10 minutes reaction.

## Chemical Characterization of Complexation Behavior of Pertechnetate with Cysteine

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### ABSTRACT

The labeling behavior of cysteine with  $^{99}\text{TcO}_4^-$  ion and/or  $^{99\text{m}}\text{TcO}_4^-$  ion at different cysteine concentrations reductant and pH values has been studied by chromatography, and the labeling yield was calculated. Three major Tc-complexes, yellow, reddish brown and green can be separated by gel filtration chromatography (GFC). Thin layer chromatography (TLC), high performance liquid chromatography (HPLC) and ion-exchange chromatography (IC) were used to separate the complexes collected from GFC. The TLC, HPLC data show the pertechnetate accompanied with a yellow complex; the green and purple complex contain more than two complexes. Electrophoresis and IC data show that the complexes carry a negative charge. The conductivity, UV-VIS, flow beta-detector with HPLC and autoradiography are also applied to analyze complex formation.

## Radio-High Performance Liquid Chromatographic Study on Radioactive $^{38}\text{Cl}$ Compounds

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### ABSTRACT

Reaction of recoil  $^{38}\text{Cl}$  atoms with o-dichlorobenzene in the presence of carbon tetrachloride or iodine has been studied by using radio-high performance liquid chromatography. The major products were detected by 4-channel-wavelengths spectrophotometric detector. The radioactivity of  $^{38}\text{Cl}$  compounds including minor products was measured with a NaI(Tl) scintillation detector. The main products found were  $^{38}\text{Cl}$  labeled  $\text{HCl}/\text{Cl}_2$ ,  $\text{CHCl}_3$ ,  $\text{CCl}_4$ , o-, p-, m- $\text{C}_6\text{H}_6\text{Cl}_2$  and polymer, whereas only minor products such as  $\text{HCl}/\text{Cl}_2$ ,  $\text{CHCl}_3$ ,  $\text{C}_2\text{Cl}_6$ ,  $\text{C}_6\text{H}_3\text{Cl}_3$ , and polymer were found in the radio-chromatogram. The reaction mechanisms of recoil  $^{38}\text{Cl}$  atom are briefly described.



## Preparation of [ $^{131}\text{I}$ ] Lipiodol as a Hepatoma Therapeutic Agent

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### ABSTRACT

An isotopic exchange method was used to label lipiodol with  $^{131}\text{I}$ . The labelling efficiency was  $<92.5\%$ , and the radiochemical purity of [ $^{131}\text{I}$ ] lipiodol was above 98% as determined by ITLC. The influencing factors e.g. the heating temperature, reaction time, pH and storage conditions were studied and the optimum conditions were determined.

In a pilot study injecting [ $^{131}\text{I}$ ] lipiodol for the treatment of hepatoma, about 70% of hepatoma patients had a response to the treatment with a reduction of  $\alpha$ -fetoprotein and decrease of hepatoma sizes. The overall median survival was 9 months (range 2-17 months).

## 我國醫院—社區精神醫療服務的發展：回顧與展望

葉英堃

第二次世界大戰後四十多年來的台灣精神醫療復健服務尤其與社區的結合關係按其重大改變特徵可分為三個時期。第一時期是 1970 年以前。是台大精神科一手扮演領導角色，在教學、人員培養、研究有重大的貢獻外，進而推行各項社區心理保健的實驗以穩固了其後發展的基礎。第二時期是 1971-1980 年時期。這時期可稱為台北市療推行其所謂台北市療模式的發展階段，台北市療模式的特徵是在多元化醫療復健模式的開發中，積極伸長其照顧輸送系統到社區，並與社區內有關資源建立工作網以納入社區內醫療服務為其整個醫療復健、保健的服務網路的一環以期給予病患與家屬整體性、連續性的服務及照顧。在本篇特地詳細報告其社區精神醫療服務工作系統及工作網的發展各階段。台北市療模式的發展可使台北市建立精神醫療、保健服務工作網的構想，而成為常被國內、外精神醫療界注意的引用的範例。第三期是 1981 年以後是受種種因素背景的影響精神醫療、保健成為中央、地方政府社會福利政策上要優先加強辦理的工作，是台灣精神醫療保健全國性發展的時期，也是歷史上空前而向前邁進、突破性一大步的時期。行政院衛生署所提出的十五年發展計劃，其配合預算的迅速大量膨脹度實令人矚目。在衛生署積極推行的醫療服務中，社區醫療服務模式最被強調，而台北市醫療的模式常被引用。「精神衛生法」於 1990 年 12 月公佈實施後台灣精神醫療界進入空前的富有生動、機會與希望的時期，但著者指出由於許多因素同時也有不少矛盾與障礙需要克服、突破。著者結論台灣傳統的醫療服務模式包括社區醫療是「醫院為基礎」的模式，而「社區為基礎」的醫療復健服務模式是我國應努力發展的目標。

# Neurasthenia in Taiwan. A Diagnostic Entity or Destigmatized Paradigm of Mental Disorders?

Eng-Kung Yeh

## ABSTRACT

This is one of the eight papers invited from East Asian countries and United States by the editor to contribute to the special volume on "Neurasthenia Revisited" in Psychiatric Annals. The author has found the diagnosis "neurasthenia" has been very scanty in the psychaitric practice presumably due to the influence of DSM-III in Taiwan during the past several years. Furthermore the term "neurasthenia" has been more often used among the non-psychiatric professionals as the destigmatized paradigm of mental disorders rather than as disease entity. In order to establish neurasthenia as a disease entity, the author emphasized the need of careful study with well-validated and culture-sensitive diagnostic shedule.

## The Changing Rate of Major Depression

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### ABSTRACT

**Objective.**—To estimate temporal trends in the rates of major depression cross-nationally.

**Design.**—Nine epidemiologic surveys and three family studies.

**Setting and Participants.**—Approximately 39000 subjects in population-based samples from nine epidemiologic surveys, and 4000 relatives from three family studies that were conducted independently but using similar methodology in the 1980s in North America, Puerto Rico, Western Europe, the Middle East, Asia, and the Pacific Rim.

**Outcome Measures.**—Age at first onset of major depression by birth cohort and time period.

**Results.**—There was an increase in the cumulative lifetime rates of major depression with each successively younger birth cohort at all sites with the exception of the Hispanic samples, in whom the rates in the older cohort (1915 through 1935) were approximately equal to those of the younger cohorts. However, results of fitting statistical models that separate period and cohort effects showed an overall increase in the rates of major depression over time over all countries, although the magnitude of the increase varied by country. The average relative risk of major depression between a particular cohort and the cohort born immediately before varied between 2.6 (95% confidence interval, 1.8 to 3.7) in Florence, Italy, and 1.3 (95% confidence interval, 1.2 to 1.4) in Christchurch, New Zealand. Short-term fluctuations in the rates of major depression during specific time periods and in specific cohorts also varied by country.

**Conclusions.**—Cross-nationally, the more recent birth cohorts are at increased risk for major depression. There are, however, variations in the long- and short-term trends for major depression by country, which suggests that the rates in these countries may have been affected by differing historical, social, economic, or biological environmental events. The linking of demographic, epidemiologic, economic, and social indices by country to these changes may clarify environmental conditions that influence the rates of major depression.

## Studies on the Synthesis of Isoquinolines as Potential $\beta$ -Adrenergic Blocking Agent

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### ABSTRACT

Based on structure-activity relationship study on higenamine (1) in the previous paper, two isoquinolines, coclaurine (2) and isococlaurine (3) were shown to have weak  $\beta$ -adrenergic blocking activity. Now the catecholic hydroxyl moiety on higenamine (1) was replaced by more lipophilic substitutions. Four benzylisoquinoline derivatives, ( $\pm$ )-norcinamolaurine (17), ( $\pm$ )-N-norarmepavine (18), 1-(p-hydroxybenzyl)-1,2,3,4-tetrahydrobenzo [h] isoquinoline (24) and 1-(p-hydroxybenzyl)-6,7-dichloro-1,2,3,4-tetrahydroisoquinoline (29) were synthesized by the Bischler-Napieralski and Reissert reactions. The results of the pharmacological evaluation of the compounds 17, 18, 24 and 29 on the  $\beta$ -adrenergic tissue of the left atria indicated that compounds 17, 18 and 29 did antagonize the  $\beta$ -receptor at high concentration. However, these blockers were much less active than propranolol.

**Key words:** Higenamine; ( $\pm$ )-Norcinamolaurine; ( $\pm$ )-N-Norarmepavine; 1-(p-Hydroxybenzyl)-1,2,3,4-tetrahydrobenzo [h] isoquinoline; 1-(p-Hydroxybenzyl)-6,7-dichloro-1,2,3,4-tetrahydroisoquinoline;  $\beta$ -Adrenergic receptor antagonist.

## Disposition of asarone after intravenous administration to rabbits assessed using HPLC

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### ABSTRACT

A simple and sensitive high-performance liquid chromatography (HPLC) method for the determination of asarone in rabbit plasma has been developed. Up to 0.1 mL of plasma containing asarone was deproteinated by acetonitrile, which contained an internal standard (indomethacin). The supernatant was injected into a Nucleosil 7C18 column using acetonitrile-water-triethylamine (55:45:0.1 v/v, pH 5.4-5.5, adjusted with orthophosphoric acid) as the mobile phase and UV detection at 257 nm, followed by UV spectrum identification (between 200 and 380 nm) with a photodiode array detector. The method is rapid, easily reproduced, selective and sensitive. It was applied to pharmacokinetic studies of asarone in rabbit, after 5, 10, or 20 mg kg<sup>-1</sup> intravenous administration. Rapid distribution followed by a slower elimination phase was observed from the plasma concentration-time curve. The plasma disposition at each dose fitted well to a two-compartment open disposition and the terminal disposition became much slower as the dose was increased, suggesting a nonlinear dose-dependent plasma asarone disposition.

## Ceruloplasmin: A Copper-Containing Glycoprotein

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### ABSTRACT

The study on ceruloplasmin in many aspects has been promising since Holmberg and Laurell first isolated and characterized it in 1948, 20 years after the essentiality of copper has been established. The review on this subject tends to give information regarding the composition and structure of ceruloplasmin; functions of ceruloplasmin; how does ceruloplasmin deliver copper to cells; tissues in which ceruloplasmin is synthesized; synthesis/secretion of ceruloplasmin; factors influencing ceruloplasmin synthesis in liver; properties of ceruloplasmin; ceruloplasmin receptors and ceruloplasmin determination (assay, analysis, or measurement) as well.

**Key words:** Ceruloplasmin, copper-containing enzyme, copper-containing protein, copper-containing glycoprotein, ferrioxidase, ceruloplasmin receptor, copper homeostasis, ceruloplasmin gene, ceruloplasmin determination (assay, analysis, measurement)

## Effects of Alkylidenephthalides on the Pituitrin-induced Alternations in Isolated Guinea Pig Hearts

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Butylidenephthalide, a constituent of *Ligustricum wallichii* Franch. (Umbelliferae), proved to be the most important and active in antispasmodic effects. In order to study the influence of the length of alkylidene-group on its antispasmodic effect, we have synthesized four alkylidenephthalides, ethylidene-, propylidene-, butylidene- and pentylidene-phthalide. The present investigation is an attempt to understand the effects of these four on the pituitrin-induced decrease of coronary flow, contractility and heart rate in the isolated guinea pig hearts.

Butylidenephthalide, like nitroglycerin but unlike aminophylline, significantly overcame the pituitrin-induced decrease in coronary flow. Aminophylline non-significantly but slightly increased the contractility and heart rate. Nitroglycerin significantly decreased the heart rate but not contractility. Butylidenephthalide, however, significantly decrease both, the heart rate and contractility. Therefore, butylidenephthalide may decrease more demand of oxygen consumption than nitroglycerin in myocardium of the isolated preparations.

The above results suggest that butylidenephthalide may be an useful antianginal drug owing to its high crude therapeutic ratio (Table 1). Recently we also reported the drug inhibited platelet aggregation by inhibition of cyclooxygenase and interference of calcium mobilization.

**Key words:** Butylidenephthalide, *Ligustricum wallichii*, guinea pig heart, coronary flow, heart rate, contractility.



## Effect of Intra-Raphe Injection Amino Acids on Cardiovascular Function in Rats

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### ABSTRACT

The effects of microinjection of an excitatory amino acid (glutamate, 10  $\mu$ g) or several inhibitory amino acids (taurine 10  $\mu$ g, GABA 10  $\mu$ g or glycine 10  $\mu$ g) into the dorsal raphe region on cardiovascular function were assessed in rats under pentobarbital sodium. Intraraphe administration of glutamate, but not saline, caused an increase in the mean arterial pressure. By contrast, intra-raphe administration of taurine, GABA or glycine, but not saline, caused a decrease in both the mean arterial pressure and the heart rate. The glutamate-induced hypertension or both the hypotension and the bradycardia induced by taurine, GABA or glycine was antagonized by pretreatment with intra-raphe injection of a serotonergic receptor antagonist (1  $\mu$ g cyproheptadine). In addition, the vasopressor and bradycardia responses to an intravenous dose of epinephrine (2.5  $\mu$ g/kg) were assessed in saline-treated rats and amino acid-treated rats. Intra-raphe injection of glutamate produced a significant decrease in reflex bradycardia compared to the controls. On the other hand, administration of taurine, GABA or glycine into the dorsal raphe region led to an enhancement of epinephrine-induced bradycardia. Again, the reduction or the facilitation of the epinephrine-induced bradycardia following administration of these amino acids was antagonized by pretreatment with cyproheptadine. The results suggest that the serotonergic receptor mechanisms in the dorsal raphe region play a role in the elaboration or modulation of the cardiovascular responses to amino acids (including glutamate, taurine, GABA and glycine).

**Key words:** amino acids, reflex bradycardia, arterial pressure, heart rate, dorsal raphe nuclei, serotonin, brain.

## The Effect of Exogenous Dopamine on Ileal Smooth Muscle of Guinea-Pigs

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### ABSTRACT

In the isolated ileum of guinea-pig, treatment with dopamine produced a lowering of muscle tone in a dose-dependent manner. Dopamine-induced relaxation at low concentration was reversed by haloperidol, the specific antagonist of dopamine receptors. The relaxations by dopamine induced at concentration of 1  $\mu$ M or higher were abolished by haloperidol with propranolol. At the concentration sufficient to block  $\beta$ -adrenoceptors, propranolol attenuated this relaxation by dopamine at high concentrations. Similar results were also observed in tissues concerning the dopamine-stimulated formation of cyclic AMP. Mediation of dopamine receptor and  $\beta$ -adrenoceptor in this cyclic AMP-related relaxation can thus be considered. Failure of sulpiride, an antagonist of dopamine DA-2 receptors, to reverse the actions of dopamine ruled out the participation of DA-2 receptor. Otherwise, SCH23390, the blocker of dopamine DA-1 receptors, reversed the responses to dopamine at low concentration only. Actions of dopamine induced at high concentration were disappeared in the presence of SCH23390 with propranolol. Thus, the obtained data suggest that dopamine induced relaxation of ileal smooth muscle through an activation of dopamine DA-1 receptors and/or a stimulation of  $\beta$ -adrenoceptors at the concentrations over 1  $\mu$ M to result in an increase of cyclic AMP in guinea-pigs.

**Key words:** dopamine, receptor subtypes,  $\beta$ -adrenoceptors, ileum, relaxation, cyclic AMP, guinea-pig.

## Pharmacological Characterization of $\alpha_2$ -Adrenoceptors in Isolated Jejunum of Rabbits

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### ABSTRACT

In the isolated jejunum of rabbits, norepinephrine (NE) lowered the muscle tone in a dose-dependent manner which was potentiated by yohimbine, an antagonist of  $\alpha_2$ -adrenoceptors. Guanethidine and/or bretylium, the adrenergic neuron blockers, attenuated this action of yohimbine, indicating the participation of neuronal  $\alpha_2$ -adrenoceptors. In the presence of guanethidine and atropine, clonidine and guanabenz reduced the relaxative responses to forskolin, but they did not modify the responses to dibutyryl cAMP. The inhibition mediated by these  $\alpha_2$ -adrenergic agonist was abolished by pertussis toxin, an inhibitor of Gi protein. The actions of clonidine and guanabenz were also blocked by yohimbine and/or rauwolscine. Thus, the Gi protein mediated inhibition of adenylate cyclase by post-synaptic  $\alpha_2$ -adrenoceptors in muscle cells can be considered. The obtained data indicated that  $\alpha_2$ -adrenoceptors are presented in adrenergic nerve terminals and smooth muscle of jejunum of rabbits to function as the feed-back autoreceptors in autonomic neurotransmission.

**Key words:**  $\alpha_2$ -adrenoceptors, adrenergic nerve terminal, smooth muscle, jejunum, rabbits.

## Mechanisms of Adrenaline-Induced Antinociception in Mice

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### ABSTRACT

Infusion of adrenaline into the upper lumbar subarachnoid space in lightly anesthetized mice produced a significant elevation of the nociceptive threshold as quantitated by tail flick test. The antinociceptive effect of adrenaline was dose-dependent and antagonized equally by pretreatment with either alpha-1 selective antagonist prazosin or alpha-2 selective antagonist yohimbine at a dose of  $0.05 \mu\text{g}/5 \mu\text{l}/\text{mouse}$ . This antinociceptive effect of adrenaline was also blocked pretreatment with beta antagonist propranolol or opiate antagonist naloxone at higher doses, i.e.,  $0.5 \mu\text{g}$  and  $1.0 \mu\text{g}/5 \mu\text{l}/\text{mouse}$ , respectively. These results suggest that the antinociceptive mechanisms of adrenaline at the lumbar spinal level in the mouse seem to be mediated not only through alpha-and beta-adrenergic pathways but also through opiate system.

**Key words:** adrenoceptor, antinociception, intrathecal injection, tail flick latency, mice.