1834th Conference Ethnopharmacology & Oncology Pharma 2018









Pharmacology and Ethnopharmacology International Conference on Pharmaceutical Oncology

July 18-19, 2018 | Atlanta, USA

Poster Presentations

Day 2

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Baicalin administration has a protective effect on Hyperglycemia-induced malformation of cardiovascular system

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Aims: Baicalin is a traditional Chinese medicine for tocolysis. Whether it can protects early embryonic cardiovascular development caused by gestational diabetes is obscure, and the mechanism remains unclear. In this research, early chicken embryo was used as a model to explore the molecular mechanism of baicalin in reducing the early cardiovascular developmental deformity caused by high glucose environment.

Methods: We found that $6\mu M$ baicalin administration can attenuate the death rate and retardation of chicken embryos caused by high glucose environment significantly. Thus, we observed the chick embryos in HH7, HH8, HH10, HH11stages, which are treated with simple saline, high glucose (50 mM) and/or Baicalin (6 μM). In this study, we used immunofluorescence, situ hybridization, RT-PCR, Western blot, qPCR and others to observe the expression of the key transcription factors, and the changes of autophagy-related genes, apoptosis-related genes, ROS in the development of cardiovascular so that to study whether or not Baicalin could attenuate hyperglycemia-induced malformation of cardiovascular system and the mechanism. At the same time, we studied the mechanism involving ROS, autophagy and apoptosis, combined with HUVEC cell. In addition, we also used Baicalin to treat the mice in diabetes model induced by Streptozotocin(STZ) and observed whether or not this has the protective impact on the blood glucose and other organs of diabetes mellitus mice.

Results: Hyperglycemia-enhanced cell apoptosis was reduced in embryos and HUVECs in the presence of Baicalin. Hyperglycemia-induced excessive ROS production was inhibited when Baicalin was administered. Analyses of classical antioxidant enzymes, MQAE and GABAA suggested Baicalin plays an antioxidant role in chick embryos possibly through suppression of outwardly rectifying Cl(-) in the high-glucose microenvironment. What's more, hyperglycemia-enhanced autophagy fell in the treatment of Baicalin, through affecting the ubiquitin of p62 and accelerating autophagy flux. Both Baicalin and Vitamin C could reduce apoptosis, but CQ did not, suggesting autophagy to be a protective function on the cell survival. In mice, Baicalin decreased the elevated blood glucose level caused by STZ.

Conclusions: In brief, these data suggest that hyperglycemia-induced embryonic cardiovascular malformation can be attenuated by Baicalin administration through suppressing the excessive production of ROS and autophagy. Baicalin could be a potential candidate drug for women suffering from gestational diabetes mellitus.

Biography

Jian-Xin Liang has completed his undergraduate course from the Hubei University of Chinese Medicine. Now she is completing her master study in Jinan University School of Medicine. She has published 2 papers, including "Atg7-mediated autophagy is involved in the neural crest cell generation in chick embryo" Molecular Neurobiology, and "BRE modulates granulosa cell death to affect ovarian follicle development and atresia in the mouse." Nearly for 2 years, she has been doing research about the impact of baicalin on the heart and vascular development of embryos, which are in the PGDM (previous gestational mellitus) environment.

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Antibacterial activity of Commiphora gileadensis and *Abutilon bidentatum*, collected from Al-Abwa region, Saudi Arabia

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Different plants have been traditionally used in folkloric medicine to treat many diseases and disorders or to improve human health due to their secondary metabolites which have excellent antimicrobial activities. *Commiphora gileadensis* and *Abutilon bidentatum* were collected from Al-Abwa region, Saudi Arabia, identified, extracted and their antibacterial activity was determined by agar well diffusion method. Extraction by methanol, ethanol, acetone and hot water was carried out and some multidrug-resistant bacteria were used as test bacteria. Maximum activity was recorded for the methanolic extract against all tested bacteria with inhibition zone diameter ranged from 31-35 mm and MIC was ranged 37.5 µg/ml. The lowest activities were recorded for the water extracts of the two plants *Commiphora gileadensis*, and *Abutilon bidentatum*. *Abutilon bidentatum* extract showed weaker antimicrobial activity against the tested bacteria compared to *C. gileadensis* leave extracts. It is noticed that *C. gileadensis* stem extracts showed stronger antimicrobial activity. The methanolic extracts of the two tested plants have no toxicity using *Artemia salina* as a test organism. In conclusion, *C. gileadensis* and *A. bidentatum* can be traditionally and safely used against multidrug-resistant bacteria due to the efficient antimicrobial activities and low toxicity.

Biography

Amal Y Aldhebiani, associate professor in Plant Taxonomy, Biological Sciences Dept. Jeddah, Kingdom of Saudi Arabia. PhD from University of Reading, United Kingdom. Research interest in Flora of Saudi Arabia and medicinal plant in the country, their taxonomy and uses. Phytochemical compounds analysis and their application. Genetic diversity among medicinal plant and how would that affect the chemical constituents and the environmental relation.

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Assessment of herb drug interaction study of Sitagliptin in combination with curcumin

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Nurcumin is the principal curcuminoid of turmeric. It possesses antioxidant, antidiabetic, anticancer, antiviral, antifungal, antibacterial, and anti-aging activities. It is mainly metabolized by CYP3A4, CYP1A2, and CYP2C9 enzymes. Sitagliptin is an oral antihyperglycemic agent, belongs to class DPP-4 inhibitor. It is metabolized by CYP3A4 and CYP2C8 enzymes. In the drug interaction study of curcumin with sitagliptin, diabetes was induced in the albino wistar rats intraperitoneally using 55 mg/kg Streptozotocin (STZ). Then they were divided into four groups of six each. Group, I treated with sitagliptin (10 mg/ kg), group II treated with curcumin (80 mg/kg), group III treated with curcumin followed by sitagliptin and group IV treated with curcumin for 7 days and on the eighth day followed by sitagliptin. Blood samples were collected from an orbital puncture at time intervals between 0, 1, 2, 4, 8, 12, and 24hrs using heparinized capillaries. Different biochemical parameters were estimated by using respective methods for 28 days. The obtained pharmacokinetic data shows an increase in C_{max} , T_{max} , AUC total, AUC0-n, t½, MRT and decrease in Vd and CL in both normal and diabetic rats. In pharmacodynamic study group IV showed a decrease in serum glucose levels at all time points. There was a very significant (p<0.001) influence in the percentage of glucose reduction in diabetic rats under multiple dose treatment but less significant (p<0.05) influence in normal rats. Thus, the improved pharmacokinetic parameters of sitagliptin were more observed in the multiple dose treatment groups, and the improvement of pharmacodynamics was significant in only diabetic rats under multiple dose treatment. This may be due to the synergistic effect of curcumin and sitagliptin by inhibition of CYP3A4 in STZ induced diabetic rats. Hence sitagliptin dose may require special attention if used along with curcumin or herbal preparations containing curcumin to avoid complications.

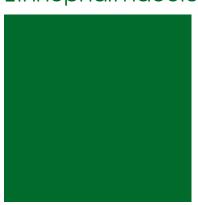
Biography

Jyothi Penta completed her Ph.D in Pharmaceutical sciences from Kakatiya University. She completed masters and bachelors from Kakatiya University. Her research work was focused on herb-drug interaction studies based on pharmacokinetics and pharmacodynamics in rat models. Biochemical parameters and pk/pd modeling was done to estimate the interaction between anti diabetic drugs and Phyto chemicals.

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Accepted Abstracts

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Ameliorative effect of ethanolic extract of Annona muricata against sodium arsenite: Induced hepatotoxicty in Wistar rats

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Ingestion of arsenic in drinking water causes cancer in multiple tissues and there is no cure. Cancer has become a great monster to the human race, as it places a significant emotional and economic burden on families and governments all over the world. For the management of arsenicosis, research is directed at chemoprevention using medicinally. In this study, we evaluated the *in-vitro* antioxidant and protection offered by Annona muricata L. (AM) against sodium arsenite-induced hepatotoxicity in rats. Antioxidant and radical scavenging activities of AM were compared to vitamin C and Butylated Hydroxytoluene (BHT). Proximate and phytochemical analyses were also carried out. Hepatoprotective study was investigated with six groups of rats that received distilled water (Control), 5.0 mg/kg bwt (body weight) of NaAsO₂, 250 mg/kg bwt AM, 500 mg/kg bwt AM, NaAsO₂ plus 250 mg/kg AM, NaAsO₂ and 500 mg/kg AM. The NaAsO₂ was given once on days 7, 14 and 21, while AM was administered orally daily for 21 days. Serum transaminases and alkaline phosphatase activities were determined and liver histopathology carried out. AM contained 2.00% ash, 1.94% crude fat, 25.65% crude fibre, 2.88% protein and 58.62% carbohydrate. Phytochemical analysis indicated the presence of alkaloids, flavonoids, and cardiac glycosides. The reducing power and metal chelating ability were in the order Vitamin C > BHT > AM, while for DPPH scavenging ability AM > Vitamin C > BHT. The NaAsO₂ significantly (p < 0.05) increased the liver function enzymes relative to control. However, reduction of the marker enzymes and restoration of the severe vacuolation of hepatocytes in the NaAsO₂ group to near normal is being markedly done with the help of AM treatment. Our findings suggest that AM may constitute a remedy against arsenic-induced hepatic injuries.

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Decision-making of cancer patients about end-of-life: The lived experience

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Understanding the perception of an end-stage cancer patient about end-of-life decision making can help the patient's relatives, healthcare providers, and the person himself or herself in attaining the best quality of life in their exit event. The aim of this study is to deeply gain an understanding of the voice and feelings of stage 4 cancer patients in making decisions for end-of-life. The study was conducted using a qualitative phenomenological approach. Five participants who are of sound mind and able to make rational decisions shared their preferences. The participants were selected using a non-probability, criterion, purposive sampling. Data were gathered through the use of a semi-structured interview. Four major themes emerged from the analysis of the data. The themes were leaving protracted misery, divesting the burden, feeling of complacency and living in a former time. These themes encircle mainly on the issue of a cycle of suffering and prolonging one's agony with the use of life-saving measures which can reduce the quality of life. Findings of the study revealed that end-of-life decision making is encapsulated with different factors which include physical discomfort and exhaustion, emotional distress, spiritual dilemma and financial burden. Recommendations include educational training for nurses about end-of-life care and discussion of ethical issues, culturally competent care, and management of patients who are facing end-of-life decision making. It is also recommended that physicians should take the lead and explore the end-of-life preferences of patients and their families.

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Isolation and identification of antifungal compounds from turmeric (Ryudai gold) and their activities against Fusarium solani

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R (Curcuma spp.) has numerous biological activities including anticancer, antibacterial, antifungal and insecticidal properties. There are more than 80 species of turmeric and 70 strains/varieties of Curcuma longa with different chemical properties which may possess different activities. Fusarium solani sensu lato (FSSL), pathogenic fungal species, causes several diseases in human, animals, and plants. To date, there has been no report that addresses the effect of turmeric on F. solani. Therefore, we evaluated antifungal activities of 3 Curcuma longa strains (Ryudai gold: RD, Okinawa ukon, and BK2), C. xanthorrhiza, C. aromatica, C. amada and C. zedoaria on 4 isolates of FSSL derived from American manatees (Trichechus manatus) with 3 different genotypes. The methanol extract of all turmeric inhibited fungal growth concentration-dependently. Among different species and varieties of turmeric, Curcuma longa (Ryudai gold) had a highest inhibitory effect on fungal growth. For this, Ryudai gold was chosen for isolation of antifungal compounds using silica gel column and high-performance liquid chromatography. Structural identification of the antifungal compounds was conducted using ¹H NMR, ¹³C NMR, and liquid chromatography-tandem mass spectrometry. The purified antifungal compounds were curcumin (1), demethoxycurcumin (2), bisdemethoxycurcumin (3) and (E)- α -atlantone (4). The order of the IC α 0 against F. solani was curcumin (65-76 α 1 M) > demethoxycurcumin (76-88 α 1) > (E)- α 2-atlantone (91-118 α 2) > bisdemethoxycurcumin (711-746 α 2). The results suggested that turmeric strain Ryudai gold developed by the University of the Ryukyus showed excellent antifungal activities against FSSL and could be used for an antifungal agent.

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Sigma- $2(\sigma_2)$ receptor ligands as potential anticancer agents for pancreatic cancer

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Pancreatic cancer is the fourth leading cause of cancer-related mortality amongst all cancers. The overall 5-year survival rate is 6% and the total cost of treatment is estimated to be 4.9 billion dollars per year in the United States. One major obstacle in the treatment of cancer is the development of selective chemotherapeutic agents. Sigma receptors, particularly the sigma-2 subtype, have emerged as an interesting target for the design of treatments for various cancers. They are overexpressed in rapidly proliferating cancer cells. Hence, sigma-2 receptor ligands may represent a platform for chemotherapeutics of pancreatic and other types of cancers. We recently synthesized a series of modified compounds and determined their affinity to various receptors. Binding studies show that compound 23 favorably interacts with sigma-2 receptors ($K_i = 2.7 \text{ nM}$). Evaluation of the cytotoxic effects of these compounds on various pancreatic cancer cell lines is ongoing.

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Comparing anticonvulsant effects of viola extract and carbamazepine on mice model of PTZ-induced seizure

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The seizure is a set of central nervous system disorders which appears as sudden, fleeting, recurrent and unpredictable convulsions with sensorimotor and autonomic origin. Various chemical drugs are used to treat seizure and its following convulsions. These drugs have side effects and also a long-term use of them causes medicinal resistance. Viola has been used in traditional medicine to cure convulsion. Ease of use of medicinal plants and their popularity has provided fertile ground for the use of them. In view of the prevalence of seizure and side effects of chemical drugs such as carbamazepine, this study was carried out to compare anticonvulsant effects of viola and carbamazepine on an animal model of seizure. Forty laboratory mice were being chosen and further divided into five groups: control, carbamazepine, and viola extract in 50, 100, and 200 mg/kg doses and these laboratory mice were being injected intraperitoneal one hour before pentylenetetrazole injection. Studied factors were: lack of animal's responding, duration of tonic, clonic and generalized convulsions and percentage of mortality. According to results, viola in 50 mg/kg dose was different from control group only in tonic-clonic stage and total convulsion time but 100 and 200 mg/kg groups showed significant differences from the control group in all stages (p<0.05). Mortality of 200 mg/kg group was also less than other groups which show a protective effect of viola extract. On the whole, hydroalcoholic extract of viola flower in 200 mg/kg dose can be proposed as an effective medication for preventing convulsion of an animal model.

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Acute and subacute toxicity of Detarium senegalensis seed oil extract on Wistar albino rat

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The study examined about the acute toxicity and subacute toxicity effect of *D. senegalensis* seed oil on the antioxidant parameter, histology and hematological parameters of the organs of Wistar albino rat and Swiss albino mice respectively. The LD50 of the drug could not be calculated as any of the mice die during the administration. Significant reduction in body weight was observed in the group treated with 750mg/kg dose of the extract at the third week of administration (p< 0.05). There was a nonsignificant reduction in plasma protein and creatinine level while Aspartate Aminotransferase (AST) and Alanine Aminotransferase (ALT) showed a reduction but increased significantly at the highest dose of the extract (p<0.05). The levels of high and low-density cholesterol were not affected compared with the control. The hemoglobin, white blood cells and packed cell volume increased in treated animals compared to the control. The result on the effect of the extract on antioxidant parameters showed a significant increase in activity of enzymatic antioxidant compared to the control group. From the LD50, there was a clear indication that the extract is safe for use and the extract did not induce any toxic effects on the organs of the induced rats (liver and kidney).

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Pharmacutical scale and green process for the synthesis of anticancer drug Pomalidomide

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Pomalidomide (PML), chemically (RS)-4-amino-2-(2,6-dioxo-3-piperidinyl)-1H-isoindole-1,3(2H)-dione, is a small molecule analog of thalidomide developed by Celgene Corporation for the treatment of hematological and connective tissue diseases by oral administration. It is a potent second-generation oral immunomodulatory agent with antineoplastic activity, showing significant activity in multiple myeloma patients with disease refractory to lenalidomide and bortezomib. We develop a new route for the preparation of pomalidomide on the pharmaceutical scale and polymorphic form based on Celgene Corporation. The synthetic procedure starts from 4-nitroisobenzofuran-1,3-dione and 3-aminopiperidine-2,6-dione hydrochloride via a 2 step reaction resulting in a total yield of 95% with a high HPLC purity of 99.98%.

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From ethnobotany to mainstream agriculture: New crops for subsistence farmers in the tropics

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Statement of the Problem: Tropical agriculture is both failing local people and the environment with serious impacts on food and nutritional security, poverty, the global well-being of society and the planet. Addressing this problem requires a new mindset that recognizes the need to reverse the cycle of land degradation and social deprivation that drives the complex processes that result in very low and declining yields of staple food crops – creating a yield gap.

Methodology & Theoretical Orientation: To achieve this, African smallholder farmers have requested help to diversify their farming systems with new crops that produce the traditionally and culturally-important food and medicinal products that their ancestors used to gather from forests and woodlands. Cultivating these nutritious and ecologically important species producing locally marketable products creates healthier agroecosystems and income generation opportunities; as well as new business possibilities. Over the last 25 years, techniques and strategies to allow a decentralized and participatory approach to the rapid domestication of these ethnobotanically important species have been applied and implemented in over 500 communities in Cameroon.

Findings: The results have been very positive and are being increasingly adopted and up-scaled, involving some 50 species. (1) Communities can select individual trees with desirable traits from among the 3- to 10-fold intraspecific variation available at the village-level. (2) These species are high amenable to simple, low-technology horticultural techniques for cultivar development that can be implemented at the village level. (3) Participating communities have reported numerous social and economic benefits from the domestication and cultivation of these species: and, in parallel, increased staple crop yields resulting from improved soil fertility and health.

Conclusion & Significance: There are great opportunities to develop new tropical crops producing culturally important foods and traditional medicines to transform subsistence agriculture and the lives of local people and benefit the global environment.

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Research on antidote of chemical weapons known as Sodasulphanecoblamin

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🕜 odaSulphanecobalamin (Na4S5 CoC69N15H89O26) is an antidote for chemical weapons, which detoxify and decentralized the • toxic substances in any chemical based threat mainly, classical chemical agent threat categories include vesicant or blister agents (e.g., sulfur mustard), blood agents (e.g., cyanide), respiratory agents (e.g., phosgene), and nerve agents (e.g., GA or Tabun, GB or Sarin, GD or Soman, and VX) as well as lung damaging agents (Chlorine, diphosgene). It dissociate the toxic components in each chemical weapons, either nerves agent, blister agent or mustard gas to a nontoxic substance when administered and doesn't have any adverse effects unlike Atropine (which has little effect on nicotinic effect, such as muscle twitching, flaccidity) and other antidotes been tested for neutralizing or countermeasures for a particular chemical based threat. Cyanides being displaced to a free toxic compound, thiocyanocobalamin. It removes the burns when the sulfur mustard is been contacted through skin, and eye the antidote (SodaSulphanecobalamin) which is sulfur drug group (H-S) bends the mustard makes the anditodal removes mustard from the body, of which can be used as treatment for organic Arsenical. It also added the amide group of protein when used. However, in recent studies it was proven that this antidote served as a replacement for the antidote of orange agent (2, 3, 4, 7-tetra chlorobenzodioxin) which displaced millions of Vietnam citizens during the World War II and displaces chlorobenzo to sodium benzoate and saline. Though Mercury (I) oxalate is been used for this antidote for the orange agent, but we all know that Mercury is highly toxic and poisonous to the human. Nerve agents developed in the 1930s and 1940s were stockpiled during the Cold War. More recently, nerve agents have been used in the Iran-Iraq War in the 1980s, the Japanese terrorist attacks by the Aum Shinrikyo cult in 1995 and attacks in Syria in 2017. When SodaSulphanecobalamin is been used for nerves agent antidotal, it dissociates organophosphate to phosphoric acid which helps in metabolism of the body. (Na4S5 CoC69N15H89O26) is produce by dissolution of hydroxocobalamin with the decomposition of Sodium nitrite and Sodium thiosulfate, then treated with the acidified Sodium bicarbonate, which led to a faster return to baseline mean arterial pressure compared with sodium nitrite with sodium thiosulfate; however, there was no difference between the antidote combinations in mortality, serum acidosis, or serum lactate (TERTSodium1,2-diithiosulphite-3,4diiintroso Co- $\alpha(\alpha-5,6$ diimethlybenzylmizazonly)co- β -hydroxocobalamin) This Research helps to develop the concepts, therapeutic regimens and procedures for the management of chemical warfare agent casualties; developing prognostic and diagnostic indicators for chemical warfare agent casualties moreover making life-support equipment for definitive care of chemical warfare agent casualties. Using SodaSulphanecobalamin is the most effective and reliable way to treat chemical weapons. It is non-carcinogenic, non-mutagenic and non-teratogenic compound whose composition doesn't have any toxicity and health effect when administered. It can also be used as any chemical based threat.

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Ethno-medicine: Prospects and its research challenges

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Ethno-medicine research and development is an area of investigation and application which combine specialties in different fields of studies or disciplines. Herbal concoctions are used in the treatment of many animals and human diseases with some of them producing toxicity. Some *Solanaceae* such as Datura, Atropa, and Hyoscyamus (henbane) species contains large amounts of atropine, hyoscyamine and scopolamine (hyoscine). Alkaloids have potent pharmacological action and many are used daily as medicine and are potentially toxic if misused. Acute toxicity of Solanine can happen in animals that ingest excessive amounts of potato/tomato hauls (Dharmanada, 1991). *Citrus aurantifolia* (orange peel) is very popular for the treatment of stomach pains and upsets but contamination with fungal organism could occur resulting in mycotoxicosis following ingestion of the fruit. Accidental *Zygademos chlorantus* poisoning of sheep was reported by Onyeyili *et.al* (1994) after prolonged grazing. In Nigeria, the animal and human population depends on plants as the major source of food and medicine. The paper will present the current history of medicinal plants in veterinary clinical practice and animal production in Nigeria. The past and present research efforts, as well as scientific technologies for research product development and applications and the future of medicinal plants in veterinary practice, will be fully presented.

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Instability of the cell system of a cancer cell-The hypothesis of the cancerogenic hypercycle

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Due to insufficient understanding of the cancerogenic process nature, modern methods of early cancer detecting, treatment and treatment control still remain delayed. Resulting from mutagenesis and continuous generation of new cancer cell clones, these methods only react to an event that has already taken place expressed in a reuptake of invasive tumor growth or metastasis. To solve the cancer problem, a way of detecting and eliminating mutagenesis on an early state when cancerogenesis is not yet expressed in invasive growth or metastasis must be found. The key to solving the problem is to understand the nature of instability of the cancer cell system. The suggested hypothesis of the cancerogenic hypercycle interprets cancerogenesis as a dynamically unstable system of replicating cyclic processes in an open cancer cell system from the point of view of synergetics. If it is confirmed, cancerogenesis can be detected in the state when no signs of invasive growth and metastasis that can be detected by ultrasound and radiological methods have occurred yet. A system of medical measures enhancing the effectiveness of conventional cancer recidivism treatment and early detecting measures will be possible as well.

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Safety assessment: *In-vivo* anti-trpanosomal activity of methanol root extract of *Securidaca longepedunculata* in mice infected with Trypanosoma brucei

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Securidaca longepedunculata: A savannah shrub mainly found in Nigeria and used by traditional medicine practitioners. This savannah shrub shows more than one hundred medicinal indications. The study aims at assessing the safety of the plant which is 2.8 mg/kg, and its trypanocidal activity using Swiss albino mice of both sexes: The animals were randomly selected and divided weight dependently into groups of 5 mice each, consisting of three methanol extracts groups of 5%, 10%, and 20% of the extract's LD50 which is equivalent to (0.14, 0.28, and 0.56mg/kg) respectively, and also a standard control drug (diminazene aceturate 3.5mg/kg), infected and not treated group and no infection no treatment group. Except the no infection no treatment group, all other groups were infected with *T. brucei*. Invariably, each animal received inoculums of about 1.0 x 107 parasites per gram body weight through needle passage and produced parasitemia in the mice. On commencement of the medications, the methanol root extract of *S. longepedunculata* was given to the three groups in divided doses for seven days and the diminazene aceturate was given at a therapeutic dose of 3.5 mg/kg just once. All the drugs were given through intra-peritoneal routes after confirming parasitemia.

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