

Posters

Ghanshyam Mali, Int J Drug Dev & Res, Volume 12
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Pancreatic and Thyroid Cancer Related to Exenatide and Liraglutide Treatment: A Post-marketing Analysis of Spontaneous Cases Reported in EudraVigilance Database

Ghanshyam Mali

School of Pharmaceutical Education and Research, India

Background: The use of glucagon-like peptide-1 (GLP-1) analogues has been linked with the risk of pancreatic and thyroid cancer. Exenatide and liraglutide carry a boxed warning in their pack insert regarding the possible association with medullary thyroid cancer and caution regarding acute pancreatitis. Our objective was to detect from EudraVigilance database, a signal of pancreatic and thyroid cancer with exenatide and liraglutide treatments in patients with diabetes.

Method: Herein, we analyzed all spontaneous cases of pancreatic and thyroid cancer reported with exenatide and liraglutide in Eudra Vigilance database from their inception till 30th January 2020. A case/noncase method was used to detect the association, calculating proportional reporting ratios (PRRs) and their 95% confidence interval (CI) as a measure of disproportionality.

Results: There were 4349 cases of pancreatic cancer and 1697 cases of thyroid cancer in the 6,665,794 reports recorded in Eudra Vigilance during the study period. From the inception of exenatide and liraglutide, the total numbers of pancreatic cancer cases identified with them in EudraVigilance database were 222 and 313, respectively, and the total numbers of thyroid cancer cases were 36 and 53, respectively. Significant disproportionality was observed between pancreatic cancer and exenatide and liraglutide with PRR of 36.4 (95% CI, 31.8-41.7) and 42.4 (95% CI, 37.7- 47.6), respectively. Disproportionality was also observed between thyroid cancer and exenatide and liraglutide with PRR of 14.7 (95% CI, 10.5-20.4) and 17.6 (95% CI, 13.4-23.2), respectively.

Conclusion: This study based on EudraVigilance database further confirms signals for both thyroid and pancreatic cancer with exenatide and liraglutide.

Biography

Ghanshyam Mali has completed his Master of Pharmacy at the age of 24 years from Manipal University Karnataka, India and currently pursuing his PhD from Jamia Hamdard, deemed to be University, New Delhi. He has more than 5 years of experiance in Medical Writing in Pharmaceutical Organization. He has published 3 papers in reputed journals.

Hetemi Luljeta, Int J Drug Dev & Res, Volume 12
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Autism and Food Intolerance

Hetemi Luljeta
Institute of Biochemistry, North Macedonia

Introduction: The purpose for research is inspiration from one child with autism in my family, from heteroanamnesis and symptoms, I decided to do the test-the first daughter of my sister with diagnosis; autism, she had multi food intolerance, than with prof.Blyta we started with follow up panel (a big panel with more analysis: blood, urine, faecal, biochemistry also microbiology) but the first test was food intolerance for those patients. The connection between Autism and food intolerances is likely to lie in the higher prevalence of intestinal permeability that it seen in autistic patients. They have intestinal permeability, the largest protein undigested into the blood, from this process can develop food intolerance and food allergy. For food intolerance is responsible IgG or IgG4 and those antibodies reacted as adaptive immune system. The IgG antibodies then fix to the food proteins to form an immune complex in the blood stream. If the immune complex fixes to a tissue it will eventually lead to tissue damage from inflammation and specific symptoms which vary from person to person is the most important casein intolerance and gluten intolerance because from casein has a pathological mechanism of casomorphine formation also from gluten intolerance to gliadinmorphine, these findings are specific for pathologies such as Autism, delays in psychomotor, delays in speech, mood, anxiety, hyperactivity, etc. but it is another of my research on gliadinomorphine and casomorphine with Autistic children's.

Method: About 50 patients with autism diagnosis, aged from 5-9 years, have been tested in rapid blood tests for determination of specific IgG4(human) or Nutri Smart-test, DST-diagnostische system and technologien GmbH –Germany.

Results & Conclusion: The results of tests were positive 99% and those are from food intolerance Casein, Gluten, Cow's milk, Sheep milk, Goat's milk, Egg white, Egg yellow, Soy, Wheat, Peanut, Banana, Tomato, Potato, Meat mix, Legume, Almun, Hazelnut, Apple, Pineapple, Kiwi, Rye, Fish mix, Mustard, Cacao, Grain mix, Tuna, Veg mix, Lamb etc. those are the most frequent positive results with IgG 4 concentration in level 2 and 3(3 is the high level concentration). Also they have and clinic information's for gastrointestinal symptoms excessive production of gas, belching and abdominal pain, diarrhoea, gastric reflux, high rates or inflammatory bowel disease etc. Cause of food intolerance are digestive enzymes deficiency, but it can also be a secondary problem as a consequence other diseases.

Recent Publications

1. Food intolerance and Autism, ARVIN med

2. H2 breath test and lactose, fructose malabsorbtion, ACTA scientist.

3. From casein to casomorphine, from Gluten to gliadinomorphine, shows a strong association with autism ethology, and treatment. The ASD problem is food and biochemistry, these make the change of the genetic mutations- Nutritional, science and food Chemistry- on June 22-23.2020-Toronto.

Biography

She started working in Olive medical Laboratory and now she is currently working as a Resident Doctor in Biochemistry Institute Skopje, North Macedonia.

Aymen Al-Suwailem, Int J Drug Dev & Res, Volume 12
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HPLC-Fluorescence Method for the Enantioselective Analysis of Propranolol in Rat Serum Using Immobilized Polysaccharide-Based Chiral Stationary Phase

Aymen Al-Suwailem
Military Price Sultan Cardiac Center, Saudi Arabia

A stereo selective high-performance liquid chromatographic (HPLC) method was developed and validated to determine S-( )- and R-(+)-propranolol in rat serum. Enantio-meric resolution was achieved on cellulose tris (3,5-dimethylphenylcarbamate) immobilized onto spherical porous silica chiral stationary phase (CSP) known as Chiralpak IB. A simple analytical method was validated using a mobile phase consisted of n-hexane-ethanol-triethylamine (95:5:0.4%, v/v/v) at a flow rate of 0.6 mL min and fluorescence detection set at excitation/emission wavelengths 290/375 nm. The calibration curves were linear over the range of 10–400 ng mL-1 (R = 0.999) for each enantiomer with a detection limit of 3 ng mL-1. The proposed method was validated in compliance with ICH guidelines in terms of linearity, accuracy, precision, limits of detection and quantitation, and other aspects of analytical validation. Actual quantification could be made for propranolol isomers in serum obtained from rats that had been intraperitoneally (i.p.) administered a single dose of the drug. The proposed method established in this study is simple and sensitive enough to be adopted in the fields of clinical and forensic toxicology. Molecular modelling studies including energy minimization and docking studies were first performed to illustrate the mechanism by which the active enantiomer binds to the ß-adrenergic receptor and second to find a suitable interpretation of how both enantiomers are interacting with cellulose tris(3,5-dimethylphenylcarbamate) CSP during the process of resolution. The latter interaction was demonstrated by calculating the binding affinities and interaction distances between propranolol enantiomers and chiral selector.

Biography

Aymen has received Bachelor Degree of Pharmaceutical Sciences at King Saud University and undergone Military Training Courses for Post Graduate Medical Students with excellent grade. Completed Master's degree of Pharmaceutical Sciences at King Saud University and as well as received Ph.D. Currently working in Military Price Sultan Cardiac Center, Saudi Arabia.

Accepted Abstracts

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Differential effect of iodine bioorganic molecular complex on host defense in balb/c and c57bl/6 mice

Tamara Bukeyeva
Scientific Centre for Anti-infectious Drugs, Almaty

Statement of the Problem: Long experience in the use of various iodine preparations has shown that while possessing pronounced antibacterial and antiviral properties, wide-spectrum antimicrobial activity, and lacking mutagenic and teratogenic effects, they are toxic when introduced to the human body, which significantly narrows the scope of their clinical application. The search for alternative ways to solve the problem of the high toxicity of inorganic iodine compounds has led to the development of iodine-containing organic complexes. And since the 60s of the XX century, the compounds of iodine with various iodophors are being actively examined. The coordination compound of iodine with alpha-dextrin and polypeptides was synthesized at the Scientific Center for Anti-Infectious Drugs JSC, the effect of which on the phagocytic activity of granulocytes and monocytes in BALB/c and C57BL/6 mice was studied. Phagocytosis is considered as one of the major host defense function, which is a fundamental component of the innate immune response /1/. The manifestation of the phagocytic response is a significant indicator of the host antimicrobial reactivity state and overall level of its immune activity.

Materials and methods: A study was performed in the whole blood of 30 BALB/c mice and 30 C57BL/6 mice. The animals of each line were divided into 3 groups of 10 mice, including 5 females and 5 males. Two doses of the drug were used in the study: 1/20 of maximum tolerated dose (MTD) is 125 mg/kg and 250 mg/kg (1/10 MTD) of animal weight. Blood was collected on day 14 after the administration of the drug. The analysis was performed by flow cytometry, measuring the percentage of phagocytizing granulocytes and monocytes that engulfed E. coli bacteria, and phagocytosis intensity (the number of bacteria per cell by average fluorescence intensity). The average fluorescence intensity (AFI) was correlated with the number of bacteria per leukocyte and served as an indicator of the phagocytic activity of individual cells. The data obtained during the study were processed by the method of variation statistics using GraphPad Prism software, version 6.00 for Windows (GraphPad Software, La Jolla California, USA). The arithmetic mean (M) and error of the arithmetic mean (m) were calculated for each sample. The distribution was checked for compliance with a normal one using the Shapiro-Wilk test. A comparison of sample means was carried out by Student's t-test in the case of a normal distribution or by the Kruskal-Wallis test in the case of distribution other than normal. Multiple comparisons were carried out using the Dunn's and Tukey's tests.

Findings: It was shown that a new complex of iodine with bioorganic molecules upon repeated oral administration for 14 days in the examined doses did not affect the phagocytosis in BALB/c mice. It

was established that under the influence of a complex of iodine with bioorganic molecules at a dose of 125 mg/kg, significant differences from the control group were recorded only in the number of phagocytizing monocytes in C57BL/6 mice. The findings indicated that the complex of iodine with bioorganic molecules at a dose of 250 mg/kg increased the phagocytic activity of both granulocytes and monocytes in C57BL/6 mice.

Conclusion & Significance: One of the explanations for the differential effect of a new complex of iodine with bioorganic molecules on different lines of mice may be based on the genetic characteristics of these animals. Macrophages of BALB/c mice are known to be of M-2 type, which inhibits inducible NO synthesis and stimulates cell division. Macrophages of C57BL/6 mice are of M-1 type, which produces NO and inhibit cell division, and increases the cytostatic or cytotoxic activity of phagocytes /2 - 4/. According to the results of the study, we can, therefore, conclude that a new complex of iodine with bioorganic molecules enhances the cellular factors of the natural resistance in the prototype mouse strains Th1 (C57BL/6), but not Th2 (BALB/c). This, in turn, fits into the single mechanism of action of the studied complex, namely, the activation of phagocytic cells through the induction of IFN-γ production and the ability of the complex to switch T cells to the Th1-type response path.

Recent Publications

1. Hirayama D., Iida T., Nakase H. (2018) The Phagocytic Function of Macrophage-Enforcing Innate Immunity and Tissue Homeostasis. Int. J. Mol. Sci. 19:92.

2. Mills C.D. (2015) Anatomy of a discovery: M1 and M2 macrophages. Front. Immunol. 6:212. doi: 10.3389/fimmu.2015.00212.

3. Martinez F.O., Gordon S. (2014) The M1 and M2 paradigm of macrophage activation: time for reassessment. F1000Prime Reports 2014, 6:13 (doi:10.12703/P6-13).

4. Shu-Hui Su, Hsiun-ing Chen and Chauying J. Jen (2001) C57BL/6 and BALB/c Bronchoalveolar Macrophages Respond Differently to Exercise. J Immunol, 2001, 167 (9) 5084-5091; DOI: https://doi.org/10.4049/jimmunol.167.9.5084.

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Regulation and Control of the Importation, Exportation, Manufacture, Advertisement, Distribution, Sale and the Use of Medicines, Cosmetics, Medical Devices and Chemicals

Abdeen Omer

Sudan

The strategy of price liberalisation and privatisation had been implemented in Sudan over the last decade, and has had a positive result on government deficit. The investment law approved recently has good statements and rules on the above strategy in particular to pharmacy regulations. Under the pressure of the new privatisation policy, the government introduced radical changes in the pharmacy regulations. To improve the effectiveness of the public pharmacy, resources should be switched towards areas of need, reducing inequalities and promoting better health conditions. Medicines are financed either through cost sharing or full private. The role of the private services is significant. A review of reform of financing medicines in Sudan is given in this article. Also, it highlights the current drug supply system in the public sector, which is currently responsibility of the Central Medical Supplies Public Corporation (CMS). In Sudan, the researchers did not identify any rigorous evaluations or quantitative studies about the impact of drug regulations on the quality of medicines and how to protect public health against counterfeit or low quality medicines, although it is practically possible. However, the regulations must be continually evaluated to ensure the public health is protected against by marketing high quality medicines rather than commercial interests, and the drug companies are held accountable for their conducts.

Recent Publications:

1. Abdeen M. Omer (2013). Chapter 5: Regulatory privatisation, social welfare services and its alternatives, In: Advances in Medicines and Biology, Vol.72, Editor: Leon V. Berhardt, 2013 NOVA Science Publishers, Inc., pp. 69-86, New York, USA, 2013.

2. K. Ravi Shankar, N. Sita Ratna Kumari and G.V.N. Kiranmayi (2014). In vitro Study of Antioxidant and Antimalarial Activities of New Chromeno-Pyrano-Chromene Derivative, American Journal of Phytomedicine and Clinical Therapeutics, AJPCT (2)9: 1169-1176.

3. V.Velpandian, S. Elangovan, L. Naansi Agnes and M. Mohamed Musthafa (2014). Clinical Evaluation of Justicia tranquebariensis L. In the Management of Bronchial Asthma, American Journal of Phytomedicine and Clinical Therapeutics, AJPCT (2)9: 1103-1111. 2014.

4. Abdeen M. Omer (2011). The impact of the pharmaceutical regulations on the quality of medicines on the Sudanese market: importers' perspective, Prime Journals of Business Administration and Management (BAM), Vol.1, No.9, pp.295-302, Nigeria, October 2011.

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Polymeric Electrospun Fibrous Mats Enriched With Insulin and Insulin Loaded Ethosomes for the Treatment of Diabetic Foot Ulcer

Gina S. El-Feky
National Research Centre, Egypt

This study is meant to design a novel system for the treatment of diabetic ulcer. The prepared system took advantages of insulin as a localized gold standard healing therapeutic. The main aim of the presented work is to design an effective topical dual mechanistic treatment for diabetic foot ulcer through designing and preparing insulin-ethosomes-loaded electrospun fibrous mats as a sustained and efficient platform of therapy. The biodegradable electrospun mat would serve as an ideal matrix for the handling and administration of the designed system .The designed system is composed of flexible ethosomal vesicles loaded with insulin for local treatment of foot ulcer. The prepared system offered controlled rate and profile of insulin releases through duals mechanism; first; the system benefited from the excellent reported flexibility of ethosomal vesicles to pass deep along skin layers allowing gradual drug release in all affected layers and second, the fibrous mat served as an efficient and accurate mode of applying the drug carrier system and providing a new generation of the wound dressing materials which was able to alleviate much of the painful repetitive procedures of frequent changes of dressing materials. The designed system was tested in vivo on experimental animals after inducing skin wounds.

Recent Publications:

1. Gina S. El-Feky, Samar S. Sharaf, Amira El Shafei, Aisha A. Hegazy. Using chitosan nanoparticles as drug carriers for the development of a silver sulfadiazine wound dressing. Carbohydrate Polymers. 2017; 158: 11-19.

2. Gina S. El-Feky, Sally T. El-Banna, G.S. El-Bahy, E.M. Abdelrazek, Mustafa Kamal. Alginate coated chitosan nanogel for the controlled topical delivery of Silver sulfadiazine. Carbohydrate Polymers. 2017; 177: 194-202.

3. Gina S. El-Feky, Rania Farouk Abdulmaguid, Gamal M. Zayed, Rabab Kamel. Mucosal co-delivery of ketorolac and lidocaine using polymeric wafers for dental application. Drug Delivery. 2018; 25:1, 35-42.

4. Gina S. El-Feky, Gamal M. Zayed, Yaseen A. M. M. ElShaier, Fahd M. Alsharif. Chitosan-gelatin hydrogel crosslinked with oxidized sucrose for the ocular delivery of timolol maleate. Journal of Pharmaceutical Sciences. 2018; https://doi.org/10.1016/j.xphs.2018.08.015.

5. Gina S. El-Feky, Mona M. El-Naa, Azza A. Mahmoud. Flexible Nano-sized Lipid Vesicles for the Transdermal Delivery of Colchicine; In Vitro and In Vivo Investigation. Journal of Drug Delivery Science and Technology. Volume 49, February 2019, Pages 24-34.

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Antidepressant Effect of Phoenix Dactylifera via Involvement of Dopamine and Serotonin System

Hammad Ismail
University of Gujrat, Pakistan

Phoenix dactylifera (Ajwa dates) is a well-known medicinal plant found in Asian and Arab countries and it is extensively used in Muslim world due to its religious and traditional believes like prevention and cure for chronic diseases. In this study, antidepressant activity of methanolic extracts of Phoenix dactylifera fruit (PDF) and Phoenix dactylifera seed (PDS) were investigated by using tail suspension test (TST), forced swimming test (FST), open field test (OFT) and hole board test (HBT) in Sprague Dawley rats. In TST rats struggling efforts and immobility time was determined. The results represented that highest activity was recorded for PDS followed by PDF being 75% and 65% accordingly. The FST was evaluated on the basis of rats climbing and immobility time. FST exhibited similar results as shown in TST, being highest for PDS (65%) and lowest for PDF (30%). In OFT the exploration frequency, locomotory behaviour, number of frozen events and immobility time were monitored. PDS remained highest active extract with 60% antidepressant activity followed by PDF (45%). During HBT, exploratory behaviour of rats towards holes was observed and scored in terms of number of head-dips and exploration time. Both extracts showed good antidepressant activity, but maximum value was exhibited by PDS (70%) followed by PDF (65%). Quantification of dopamine and serotonin was carried out by HPLC. PDS treatment led to significant ($P < 0.05$) rise in the level of dopamine neurotransmitter in the midbrain region but PDF treatment had no significant effect on increase in dopamine level ($P > 0.05$). Collectively, present study suggests that Phoenix dactylifera can be used as an herbal drug against depression and neurobiological syndromes due to its pharmacological effects. However, further research is needed to identify and isolate those specific components which are responsible for antidepressant activity.

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General Safety Test and the Rabbit Pyrogen Test in the Quality Control of Biopharmaceuticals.

Pardo-Ruiz Z

Center for the State Control of Drugs, Equipment and Medical Devices, Cuba

The use of alternative methods to animal testing has been encouraged, thus during the last decade an increasing number of alternative approaches in the biopharmaceutical industry have been formally adopted. In this context, there is an ethical, scientific and economic discussion worldwide in relation to the reliability of the application of the General Safety Test and the Rabbit Pyrogenic Test in the quality control of biopharmaceuticals. The application of the former has been questioned because no reliable conclusions can be drawn from this test. For this reason, this assay has been removed from some pharmacopeia's and it is no longer mandatory for several Regulatory Agencies, especially after the introduction of Good Manufacturing Practices and the use of other stringent methods. In addition, in vitro alternatives for pyrogens control, such as the Monocyte Activation Test, have been developed. This alternative method mimics the human fever reactions and detects the enhancing pro-inflammatory effect of substances that are commonly found in the biopharmaceutical industry, increasing the product safety. It is known that the position of a Regulatory Authority is focused in the assurance on the safety of products; however, Cuban regulations have not yet specifically ruled on the usefulness of both tests. This work offers a scientific basis on the reliability of these tests and their role to increase or not the safety of biological products. In addition, the position of the Cuban Regulatory Authority with respect to its application in the quality control of biological products is exposed.

Recent Publications:

1. B. Garrido-Suárez, G. Garrido, M. Castro-Labrada, Z. Pardo-Ruiz, A. Bellma-Menéndez, E. Spencer, J. Godoy-Figueiredo, S. Ferreira, R. Delgado-Hernández. Anti-allodynic effect of Mangiferin in rats with chronic post-ischemia pain: a model of complex regional pain syndrome type I. Frontiers in Pharmacology 9:1119 (2018).

2. Montero-Alejo V, Corzo G, Porro-Suardíaz J, Pardo-Ruiz Z, Perera E, Rodríguez- Viera L, Sánchez-Díaz G, Hernández-Rodríguez EW, Álvarez C, Peigneur S, Tytgat J, Perdomo-Morales R. Panusin represents a new family of ß-defensin- like peptides in invertebrates. Dev Comp Immunol. 2017 Feb;67:310-321. doi: 10.1016/j.dci.2016.09.002.

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pyrogenicity tests. European Journal of Pharmaceutical Sciences 81 (2016) 18–26.

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5. Muñoz-Cernada, A., Pardo-Ruiz, Z., Montero-Alejo, V., Fernández-Cervera, M., Sosa- Testé, I., García-Rodríguez, J. Effect of Nonionic Surfactants and HPMC F4M on the Development of Formulations of Neuro-EPO as a Neuroprotective Agent. Advanced Pharmaceutical Science and Technology (2014) 1(2).

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Formulation of Effervescent and Non-Effervescent Floating Matrix Tablets of Metronidazole using Azadirachta indica Gum.

Michael Uhumwangho
University of Benin, Nigeria.

Purpose: This study was carried out to formulate effervescent and non-effervescent gastro-floating matrix tablets (GFMTs) of metronidazole using Azadirachta indica (Neem) gum (AIG).

Method: Neem gum was extracted by method previously described. Granules were prepared by wet granulation technique using the extracted neemgum at varying concentrations (2, 4, 6 and 8% w/w). The granules were compressed at an optimized compression pressure of 30 arbitrary unit on the tableting machine load scale. Tablets were evaluated for hardness, friability, floating lag time, in vitro buoyancy test and drug release profiles. Drug-excipient compatibility study was done using Fourier Transform Infra-red Spectroscopy (FTIR) and Differential Scanning Calorimetry (DSC). Scanning Electron Microscope (SEM) was used to analyze the pores and morphology of the tablets.

Results: All formulated floating matrix granules were free flowing with angle of repose and Carr's index ≤ 33.2° and ≤ 15.5% respectively. All floating matrix granules were compressible with tablet hardness ≤ 9.0 Kg/cm2.Generally, GFMTs percentage friability decreased with increase in binder concentration (≤ 0.99%). The floating lag time for the effervescent FMTs tablets ranged from 2-7 min while the non-effervescent FMTs had zero floating lag time. FTIR and DSC studies showed that the excipients and the Active Pharmaceutical Ingredient (API) i.e. metronidazole were compatible. SEM reveals the presence of pores and rough surface on the non-effervescent GFMTs while smooth surface with no pores was revealed in the effervescent formulations.

Conclusion: Gastro-floating matrix tablets of metronidazole were successfully formulated in this study using the effervescent and non-effervescent techniques and Azadirachta indica gum as a natural polymer. There was significant difference in the floating lag times ($P > 0.05$) while there was no significant difference in the in vitro buoyancy studies of the tablets formulated using both the effervescent and non-effervescent methods ($P < 0.05$).