E-Poster

Pharmaceutical Science 2022





2nd European Congress on

Pharmaceutical Science & Research

February 23, 2022

2nd European Congress on
Pharmaceutical Science & Research
February 23, 2022

Matrix interference in the compendial limit test for aluminum in citric acid used to prepare dialysis solutions

Theerasak Rojanarata
Silpakorn University, Thailand

Since the aluminum contamination in dialysate can cause toxicity in chronic kidney disease patients who undergo long-term dialysis treatments, the presence of aluminum in substances used to manufacture dialysate must be tested to ascertain that it is not higher than the allowed limit. In most pharmacopoeias, the current test for aluminum in citric acid, an ingredient of citrate-based dialysate, is carried out by concomitantly extracting a 0.2 g/mL citric acid sample solution and a 0.04 g/mL aluminum standard solution with chloroform containing.

8-hydroxyquinoline. After the fluorescence measurement of the extracts, the fluorescence intensities (F.I.) of both solutions are compared thus insuring that the F.I. of the sample solution does not exceed that of the standard aluminum solution which is used as an acceptance criterion (0.02 ppm aluminum). From our experience and that observed by other laboratories, the F.I. readout from the citric acid sample was atypically lower than that of the standard aluminum solution and even lower than the blank (water). The aim of this work was, therefore, to assess the matrix effects in the test since citric acid, which is present at a concentration >106 times higher than aluminum, might cause the interference. By constructing and comparing the two standard curves of aluminum solutions prepared in water versus in 0.2 g/mL citric acid solution, it was found that they were absolutely different in terms of slope and y-intercept. Besides, the F.I. values on the plot of the citric acid solution were much less than those of the water. In another experiment, the decrease in F.I. of the aluminum standard solution was clearly seen when the co-existing concentration of the citric acid increased. According to these findings which indicated citric acid interference, the compendial limit test for aluminum in citric acid should be revised; otherwise, it could yield underestimated results leading to misleading conclusions.

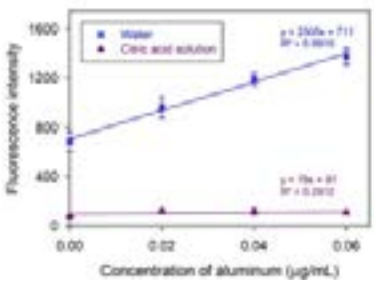


Figure 1 Standard curves of aluminum solutions prepared in water versus in 0.2 g/mL citric acid solution.

Speaker Biography

Associate professor Theerasak Rojanarata, Ph.D. works at the Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Silpakorn University, Nakhon Pathom, Thailand. His research areas are Pharmaceutical Chemistry, Pharmaceutical analysis, Green Chemistry and Development of Innovations for Pharmacy Education.

e: rojanarata_t@silpakarn.edu

Notes:

Accepted Abstracts

Pharmaceutical Science 2022





2nd European Congress on

Pharmaceutical Science & Research

February 23, 2022

2nd European Congress on
Pharmaceutical Science & Research
February 23, 2022

Site-Specific Delivery of 17β-Estradiol into the CNS

Katalin Prokai-Tatrai
University of North Texas Health Science Center, USA

The beneficial effects of estrogens in the central nervous system (CNS) are the results of the synergistic combination of their genomic and non- genomic actions, making them potential broad-spectrum neurotherapeutic agents. Owing to detrimental peripheral hormonal burden and cardiovascular liability, clinical utilization of estrogens as safe neuropharmaceuticals cannot be realized until they can be delivered specifically and selectively to the intended sites of action. In this presentation focusing on the main human estrogen 17β-estradiol (E2), we show that 10β,17β-dihydroxyestra-1,4-dien-3-one (DHED) bioprecursor prodrug produces E2 only in the CNS while remaining inert in the rest of the body (Figure 1). DHED is synthesized through the stereoselective oxidation of the phenolic A-ring of E2 to a para-quinol that is selectively re-aromatized back into E2 by a CNS-specific target enzyme. This distinguishing prodrug metabolism occurs both in male and female animals regardless of the route of administration or the duration of treatment, thereby avoiding the unwanted off-target impacts associated with direct E2 therapies, such as stimulation of the uterus. The highly localized formation of E2 from DHED in the CNS will be shown through a selected series of bioanalytical assays and efficacy studies using animal models of estrogen-responsive maladies pertaining to the brain and the retina, especially in the context of neuroprotection. DHED also exhibits profoundly more favorable physicochemical properties compared to those of the highly lipophilic parent, E2, for transport through biological membranes such as the blood-brain barrier or the cornea. Therefore, a significantly more potent estrogen therapy can be achieved with DHED, further enhancing its therapeutic safety. Altogether, our DHED-based approach shows unprecedented selectivity to deliver E2 into the CNS, and thus, promises a high translational value for the successful and safe treatments of neurodegeneration, as well as neurological and psychiatric symptoms arising from estrogen deficiency.

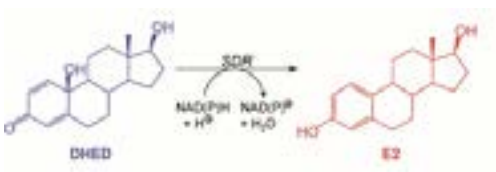


Figure 1. Schematic illustration of DHED's metabolism to E2 in the CNS. As an α,β-unsaturated carbonyl compound, DHED is a plausible substrate for a short-chain NADPH-dependent dehydrogenase/reductase (SDR) that is selectively expressed in the CNS [10].

e: Katalin.Prokai@unthsc.edu

2nd European Congress on

Pharmaceutical Science & Research

February 23, 2022

A Small Data Perspective on Trial Design: Concepting for Rare Disease Trials

Steven M. Schwartz
Tridiuum Health Individuallytics Inc,. USA

Rare diseases in the U.S. are defined as having a patient population of <200,000. Although each disease impacts a small population, there are an estimated 7,000 documented rare diseases. Since 1983, more than 600 agents treating rare diseases have reached the market and more than 500+ are currently in development. Low prevalence rates for rare diseases run contrary to tradition drug development processes. Rigorous testing the pipeline for rare conditions continues to be an industry challenge.

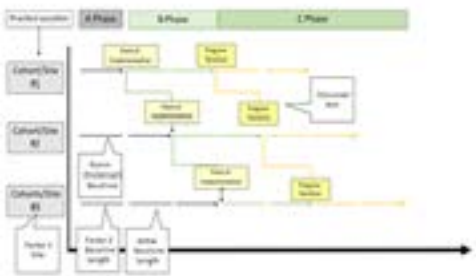
The objective of this presentation is to bring a best practice framework to the evaluation of pharmaceutical products for rare disease. This presentation covers 3 approaches, discuss general principles for when and how they should be applied, and hat limitations should be considered when developing methods. The presentation discusses the following:

1. N of 1 Trials. Trials designed, conducted, and evaluated at the level of the individual patient [8].

1. Adaptive Research Design. Trial allowing for prospective modifications based on accumulating data feedback on trial subjects [9, 10].

2. Multiple Baseline. Staggers the baseline length and onset of intervention with repeated measures across treatment conditions (each consecutive individual serves as both control and treatment) [11].

A fictionalized 3 X 2 X 2 mixed model factorial design (see Figure) example is presented to illustrate. Qualifying subjects are initially randomized into one of three varying baseline periods. At the end of baseline (A), patients are randomized a second time to condition (i.e. test article vs. a true placebo/standard of care). In the C Phase, subjects cross over to the condition not assigned in Phase B. At predetermined points, interim analyses are conducted, with a priori decision rules. The final phase is "open label" and offered only if the final analysis is supportive.



e: steve@individuallytics.com

2nd European Congress on
Pharmaceutical Science & Research
February 23, 2022

The Role of Pharmacovigilance in Oral Cancer Therapies

Ilaria Avallone
Luigi Vanvitelli University Hospital, Italy

In recent years there has been an increase in the number of anticancer drugs available in oral formulations, approved for the treatment of various cancers. Oral cancer therapy brings benefits to both the patient and the healthcare facility, medical and nursing staff costs are reduced, and the workload of the pharmacy is reduced. The oral formulation is preferred by the patient for reasons such as reduced hospital visits, reduced travel time and minimal impact on daily habits.

However, therapy with orally formulated cancer drugs is not without its problems, such as increased errors due to self-administration, reduced patient compliance and toxicities that are not always identified. This work, carried out at an I.R.C.C.S., aims to highlight the importance of reporting side effects in oral cancer therapy. The data were collected by analysing the Adverse Drug Reactions (ADRs), sent to the Local Pharmacovigilance Manager, who entered them in the National Pharmacovigilance Network.

Health workers were contacted by telephone to encourage reporting, and through consultation of a database for the management of health care processes, any reductions and/or suspensions of treatment were obtained that were configured as alerts for a report.

Results: During the study period, September 2020/July 2021, 653 adverse reactions were entered into the National Pharmacovigilance Network, of which 26% related to oral oncology drugs and 74% related to intravenous oncology therapies. The most reported oral oncology drugs were tyrosine kinase receptor inhibitors (42 %), selective cyclin-dependent kinase inhibitors (27 %), followed by chemotherapeutics with classical cytotoxic mechanism (22%) and various antineoplastic agents of the total number of reports from oral drugs, 25 % of the ADRs are serious and concern tyrosine kinase inhibitors, with adverse reactions such as skin toxicity in the form of skin rash, cardiovascular toxicity in the form of arrhythmia and generalised oedemas, haematological toxicity such as thrombocytopenia, and endocrinological toxicity such as hypothyroidism. Analysis of the results shows that oral cancer therapy is by no means free of side effects therefore it would be desirable to improve patient information in order to increase reporting, with a view to improving compliance and therapeutic adherence.

e: ilaria_avallone@libero.it