CMR College of Pharmacy, Hyderabad

News Letter, September - December 2017

FDA approves first emergency treatment for overdose of certain types of chemotherapy

The U.S. Food and Drug Administration today approved Vistogard (uridine triacetate) for the emergency treatment of adults and children who receive an overdose of the cancer treatment fluorouracil or capecitabine, or who develop certain severe or life-threatening toxicities within four days of receiving these cancer treatments. Vistogard, taken orally, blocks cell damage and cell death caused by fluorouracil chemotherapy. Patients should take Vistogard as soon as possible after the overdose (whether or not they have symptoms) or early-onset (within four days) of severe or life-threatening toxicity. The patient's health care provider will determine when he or she should return to the prescribed chemotherapy after treatment with Vistogard. Vistogard is not recommended for treating non-emergency adverse reactions associated with flourouracil or capecitabine because Vistogard may lessen the efficacy of these drugs. The safety and efficacy of Vistogard initiated more than 96 hours following the end of treatment with flourouracil or capecitabine have not been established.

The most common side effects of treatment with Vistogard were diarrhea, vomiting and nausea. The FDA granted Vistogard orphan drug designation, which provides financial incentives, like clinical trial tax credits, user fee waivers, and eligibility for market exclusivity to promote rare disease drug development. Vistogard was also granted priority review and fast track designations, which are distinct programs intended to facilitate and expedite the development and review of certain new drugs in light of their potential to benefit patients with serious or life-threatening conditions. Vistogard is marketed by Wellstat Therapeutics Corporation based in Gaithersburg, Maryland.

Submited by: Ms. A. **Preethi, Asst.Prof.**

Physics of Tablet Compression – An Overview

Compaction, an essential manufacturing step in the manufacture of tablets, includes compression i.e.,volume reduction and particle rearrangement and consolidation i.e., interparticulate bond formation. The success of the compaction process depends not only on the physico-technical properties of drugs and excipients, especially their deformation behavior, but also on the choice of instrument settings with respect to rate and magnitude of force transfer.

Compaction is an integral step for the manufacture of tablets and represents one of the most important unit operations in the pharmaceutical industry because physical and mechanical properties of the tablets, such as density or strength ,hardness, friability , are determined during this process. Dosage form integrity and bioavailability is related to the tablet compression process. The study of compression physics is of special interest in cases of high-dose poorly compressible drugs that exhibit nonlinear relationship between compression force and tablet tensile strength. These show a susceptibility towards tableting problems such as capping, lamination, sticking, and picking during scaleup on high-speed tableting machines.. The identification of tableting-related problems and establishing their relation with compaction parameters such as compaction force, punch displacement, porosity, and tensile strength, helps in understanding such complications and minimize them.

Complete understanding of compaction physics still eludes, many variables such as inherent deformation behavior of drugs/excipients, solid-state properties, and process parameters known to affect the final attributes of tablets. A complete understanding of variables of compaction process, can help a pharmaceutical scientist to design optimum formulation devoid of problems such as capping, lamination, picking, and sticking. The compactibility of the drugs, especially in case of high dose systems, is critical for successful manufacturing of tablets.

Submitted by: **Mr. Suresh Kumar, 4th year B. Pharm.**

Plantibodies

Antibodies are essential part of vertebrates' adaptive immune system; they can now be produced by transforming plants with antibody-coding genes from mammals/humans. Plants are the major sources of earth and can produce antibodies which can be used for human use without any interaction of any types so we explore plant proteins for formation of antibodies for human purpose. Although plants do not naturally make antibodies, the plant-derived antibodies

(plantibodies) have been shown to function in the same way as mammalian antibodies. Around 1990, plants were first considered as a potential host for producing antibodies and the word "plantibody" was coined. These plantibodies are formed by various methods like conventional method, cell tissue culture method, breeding and sexual crossing, transgenic seeds, targeting and compartmentalizing. These are further purified by various methods like filtration, chromatography, diafiltration, immunofluorescence, polymer fusion and further evaluated by RIA (Radioimmunoassay), ELISA (Enzyme linked immunosorbant assay), immunofluorescence, southern blot analysis, western blot analysis, northern blot analysis. We have also cited various applications of plant antibody here. Antibodies can be expressed in plants as either full-length molecules or as smaller fragments. In essence, a plantibody is an antibody produced by genetically modified plants. Antibodies, originally derived from animals, are produced in plants by transforming the latter with animal antibody genes.

The cost of antibodies produced by plants is substantially less than that from their animal counterparts. Secondly, plants are less likely to introduce adventitious human or animal pathogens compared to mammalian cells or transgenic animals, thus reducing screening costs for viruses, prions and bacterial toxins. Unlike bacterial and other prokaryotic systems, plants share a similar endomembrane system and secretory pathway with human cells. They do not trigger immune responses which animal antibodies are prone to doing when exposed to foreign/non-self agents and they also produce a relatively high yield of antibodies in a comparatively shorter time. Additionally, plants are capable of synthesizing and assembling virtually any kind of antibody molecule, ranging from the smallest antigen-binding domains and fragments to full-length and even, multimeric antibodies.

Several works have shown that soybeans, tobacco, potatoes, corn, alfalfa and similar crops are promising alternative for the production of recombinant therapeutic proteins. Leafy crops such as tobacco and alfalfa generally have the greatest biomass yields per hectare, because they can be cropped several times a year. Nonetheless, tobacco has proven to be a favorite preference as it offers numerous advantages over other plants as a host system. Tobacco grows quickly and through numerous tests, has been shown to produce comparatively large amounts of antibodies. Additionally, tobacco is a non-food/non-feed crop, which means that if grown in a greenhouse, the use of tobacco as a host would eliminate the small chance of cross-contamination.

Lastly, this important biotechnological breakthrough should be embraced in India where there is great diversity of crops and plants that can be readily explored by the pharmaceutical industry for therapeutic, immunoprophylactic, improved livestock productivity and other purposes.

Submitted by: **Dr. Ch. S. Vijayavani, Assoc. Prof.**

PROGERIA

Progeria is an extremely rare genetic disorder in which symptoms resembling aspects of aging are manifested at a very early age. Progeria is one of several progeroid syndromes. Those born with progeria typically live to their mid-teens to early twenties. It is a genetic condition that occurs as a new mutation, and is rarely inherited, as carriers usually do not live to reproduce. Although the term progeria applies strictly speaking to all diseases characterized by premature aging symptoms, and is often used as such, it is often applied specifically in reference to Hutchinson–Gilford progeria syndrome (HGPS).

Progeria was first described in 1886 by Jonathan Hutchinson. It was also described independently in 1897 by Hastings Gilford.The condition was later named Hutchinson–Gilford progeria syndrome. The word *progeria* comes from the Greek words "pro" (πρό), meaning "before" or "premature", and "gēras" , meaning "old age". Scientists are interested in progeria partly because it might reveal clues about the normal process of aging.

Children with progeria usually develop the first symptoms during their first few months of life. The earliest symptoms may include a failure to thrive and a localized scleroderma-like skin condition. As a child ages past infancy, additional conditions become apparent usually around 18–24 months. Limited growth, full-body alopecia (hair loss), and a distinctive appearance (a small face with a shallow recessed jaw, and a pinched nose) are all characteristics of progeria. Signs and symptoms of this progressive disease tend to become more marked as the child ages. Later, the condition causes wrinkled skin, atherosclerosis, kidney failure, loss of eyesight, and cardiovascular problems. Scleroderma, a hardening and tightening of the skin on trunk and extremities of the body, is prevalent. People diagnosed with this disorder usually have small, fragile bodies, like those of elderly people. The face is usually wrinkled, with a larger head in relation to the body, a narrow face and a beak nose. Prominent scalp veins are noticeable (made more obvious by alopecia), as well as prominent eyes. Musculoskeletal degeneration causes loss of body fat and muscle, stiff joints, hip dislocations, and other symptoms generally absent in the non-elderly population. Individuals usually retain typical mental and motor development.

No treatment has yet proven effective. Most treatment options have focused on reducing complications (such as cardiovascular disease) with coronary artery bypass surgery and low-dose aspirin.

Growth hormone treatment has been attempted. The use of Morpholinos has also been attempted in mice and cell cultures in order to reduce progerin production. Antisense Morpholino oligonucleotides specifically directed against the mutated exon 11–exon 12 junction in the mutated pre-mRNAs were used.

Pharmacy as a profession started in India in the early 20th Century. Since then, it has undergone many changes educationally and

professionally. Unfortunately, pharmacists in India have been reduced to selling medicines, unlike the West, where the pharmacist is responsible for dispensing medicines prescribed by the physician, and advising patients about their judicious administration. To be at par with their Western counterparts, the Indian educational and pharmacy practicing standards require extensive revision. This change would enhance the profile of pharmacists and enable them to be an integral part of the health care system. In the future, innovations in the discovery and development of newer drugs and dosage forms will be used and personalized pharmacotherapy will be propagated. The future pharmacist has to be aware of these developments to advise the physician and the patient and to be a competent partner in the health care team. Simultaneously, the drug regulatory authorities in India and medical professionals have to recognize the contribution of the pharmacist to society. Only then will the noble pharmacy profession be able to reach the level of greatness it deserves.

Submitted by: **V. V. Rajesham. Asst. Prof.**

Mossy Brain Cells Linked to Memory Loss and Seizures

A small group of cells in the brain can have a big effect on seizures and memory in a mouse model of epilepsy. According to a new study in Science, loss of mossy cells may contribute to convulsive seizures in temporal lobe epilepsy (TLE) as well as memory problems often experienced by people with the disease. The study was funded by the National Institute of Neurological Disorders and Stroke (NINDS), part of the National Institutes of Health.

The role of mossy cells in epilepsy has been debated for decades. This study reveals how critical these cells are in the disease, and the findings suggest that preventing loss of mossy cells or

finding ways to activate them may be potential therapeutic targets," said Vicky Whittemore, Ph.D., program director at NINDS.

This study would not have been possible without the rapid advancement of technology, thanks in part to the BRAIN Initiative, which has encouraged scientists to develop innovative instruments and new ways to look at the brain," said Dr. Soltesz. "It's remarkable that we can manipulate specific brain cells in the hippocampus of a mouse. Using 21st century tools brings us closer than ever to unlocking the mysteries behind this debilitating disease.

his was the first time we were able to show specifically that mossy cell activity can control convulsive seizures," said Anh Bui, an M.D., Ph.D. student at the University of California-Irvine, and first author of the paper. "These mice were missing most of their mossy cells, yet we were able to see effects just by manipulating the small number of surviving cells.

he epileptic mice had trouble with spatial memory tasks but their ability to recognize objects was unaffected. In addition, turning off mossy cells in healthy mice also led to problems with spatial memory in those animals. These findings suggest that a decrease in mossy cells may lead to convulsive seizures as well as memory deficits.

More research is needed to further understand the role of mossy cells in seizure progression as well as their effects early in the disease.

Submitted by: **Dr. Ramya Naidu, Asst. Prof.**

Stem Cells using to Create Functioning Kidney Tissue

Kidney glomeruli – constituent microscopic parts of the organ- were generated from human embryonic stem cells grown in plastic laboratory culture dishes containing a nutrient broth known as culture medium, containing molecules to promote kidney development. They were combined with a gel like substance, which acted as natural connective tissue – and then injected as a tiny clump under the skin of mice. After three months, an examination of the tissue revealed that nephrons: the microscopic structural and functional units of the kidney – had formed.

The new structures contained most of the constituent parts present in human nephrons – including proximal tubules, distal tubules, Bowman's capsule and Loop of Henle. Tiny human blood vessels – known as capillaries- had developed inside the mice which nourished the new kidney structures. However, the mini-kidneys lack a large artery, and without that the organ's

function will only be a fraction of normal. So, the researchers are working with surgeons to put in an artery that will bring more blood the new kidney.

To test the functionality of the new structures, the team used Dextran – a fluorescent protein which stains the urine-like substance produced when nephrons filter the blood, called glomerular filtrate. The Dextran was tracked and detected in the new structures' tubules, demonstrating that filtrate was indeed being produced and excreted as urine. have proved beyond any doubt these structures function as kidney cells by filtering blood and producing urine – though we can't yet say what percentage of function exists.

What is particularly exciting is that the structures are made of human cells which developed an excellent capillary blood supply, becoming linked to the vasculature of the mouse. Though this structure was formed from several hundred glomeruli, and humans have about a million in their kidneys – this is clearly a major advance.

Submitted by: **Mr. P. Narendra. Asst. Prof.**

Excess levels of Calcium in brain cells may lead to Parkinson's disease

Parkinson's disease is one of a number of neurodegenerative diseases caused when naturally occurring proteins fold into the wrong shape and stick together with other proteins, eventually forming thin filament-like structures called amyloid fibrils. These amyloid deposits of aggregated alpha-synuclein, also known as Lewy bodies, are the sign of Parkinson's disease.

Curiously, it hasn't been clear until now what alpha-synuclein actually does in the cell: why it's there and what it's meant to do. It is implicated in various processes, such as the smooth flow of chemical signals in the brain and the movement of molecules in and out of nerve endings, but exactly how it behaves is unclear.

"Alpha-synuclein is a very small protein with very little structure, and it needs to interact with other proteins or structures in order to become functional, which has made it difficult to study," said senior author Dr Gabriele Kaminski Schierle from Cambridge's Department of Chemical Engineering and Biotechnology.

In neurons, calcium plays a role in the release of neurotransmitters. The researchers observed that when calcium levels in the nerve cell increase, such as upon neuronal signalling, the alpha-synuclein binds to synaptic vesicles at multiple points causing the vesicles to come together. This

may indicate that the normal role of alpha-synuclein is to help the chemical transmission of information across nerve cells.

“This is the first time we’ve seen that calcium influences the way alpha-synuclein interacts with synaptic vesicles

There is a fine balance of calcium and alpha-synuclein in the cell, and when there is too much of one or the other, the balance is tipped and aggregation begins, leading to Parkinson’s disease.

Celebration of Pharmacists Day:

CMR College of Pharmacy, celebrated 56th National Pharmacy Week 2017 in grand manner on 21st and 22nd November 2017. On 21st November program was inaugurated by Sri. Ch Gopal Reddy, Secretary & Correspondent, CMR Group of Institutions, he emphasized the role of pharmacist by creating awareness among community towards safe and effective use of medicine. Dr. K. Abbulu, Principal address the gathering and reminded the students about the role of pharmacist for common man for better therapeutics outcome achievement. Dr. S. Anand Reddy, Manager-HR, Hetero Drugs Ltd, Hyderabad was Chief Guest of the said program. Dr. Reddy mentioned about various role of pharmacist in community and encourage the students to keep themselves fit in terms of health and mind so as to provide excellent service to the patient. The celebration was continued with various competitive programs like, elocution, poster & model preparation, drawing and quiz on this year’s theme.

On 22nd November celebration was continued with an awareness rally conducted within the Medchal city with this year’s theme “know your medicine: ask your pharmacist”. A total of 120 students and 15 faculty members participated in the rally. Students carry posters containing various awareness slogans about safe and effective use of medicine. Leaflets were also distributed highlighting the theme and importance of asking pharmacist about proper use of medicine. Circle Inspector of Medchal Police station was present on the finishing point of the rally.