REAL TIME DEGRADATION ANALYSIS OF PROMETHAZINE HYDROCHLORIDE FOR INDUSTRIAL COMPETENCE AND LEAD FINDING FOR NEW DRUG DISCOVERY

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Promethazine hydrochloride being of paramount importance for industrial competence, incurred loss due to degraded promethazine is an excruciating problem in pharmaceutical industry. Hence, there is a demanding need of promethazine batch calibration in order to find out degree of degradation thereby investigating loss of potency and/or enhancement of toxicity. In this study, we performed real time degradation analysis of promethazine hydrochloride under seasonal climatic condition for over seven years. Using column chromatography with a solvent system Chloroform: Ethyl acetate: Methanol (67:25:8), two major degradation products have been isolated. IR, NMR and MS spectroscopic data revealed that the major degradation product is 10-propyl 10-H Phenothiazine and other has been 1,4,10 trihydro-10 propyl-10H Phenothiazine. Possibly photocatalysis or hydrolytic cleavage has led to the elimination of aliphatic terminal amino group and atmospheric reduction caused hydrogenation of one of the fused phenyl ring. Calibration of the corresponding batch sample revealed 93.05% (w/w) degradation by High Performance Thin Layer Chromatography (HPTLC). Drug discovery based approach on the degradation products revealed that the first one showed promising antimicrobial activity especially against *Bascillus pumilus* and *Staphylococcus aureus*. Hence our study exhibited a proof of the concept approach for calibration of industrial bulk drug over time, a practical case study taken for promethazine, and recycling the product for newer drug discovery.

Nanotechnology

A GREEN CHEMISTRY APPROACH FOR SYNTHESIZING BIOCOMPATIBLE NANOPARTICLES

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Green chemistry has been an eye catching area of interest since the past few years. To generate nano particles with particular shapes and dimensions, various techniques including physicochemical and biological routes have been developed. The physical and chemical processes are typically expensive and require hazardous chemicals. Here came the use of green synthesis in nanoparticles as eco-friendly, cost-effective, and simple approaches.The synthesis of metal nanoparticles has been widely discussed due to their distinctive chemical and physical properties, which have many potential purposes. Extracts from plants may act both as reducing and capping agents in nanoparticle synthesis.The bio-reduction of metal nanoparticles by combinations of bio-molecules found in plant extracts (*e.g.* enzymes, proteins, amino acids, vitamins, polysaccharides, and organic acids such as citrates) is environmentally benign, yet chemically complex. The stabilizer, reaction medium, and green reducing agent are three key factors in the synthesis and stabilization of metallic nanoparticles The microbial synthesis of nanoparticles uses bacteria, fungi, and viruses; phototrophic eukaryotes including plants, diatoms, and algae; heterotrophic human cell lines and some other biological agents. It also declares the applications of these nanomaterials in a broad range of potential areas, such as medical biology, labeling, sensors, drug delivery, dentistry, and environmental cleanup.

USE OF METAL OXIDE NANOPARTICLES AS SHELF LIFE ENHANCERS OF CUT FLOWERS

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The cut flowers when kept in a vase, cellulose around the cut starts breaking down and bacteria starts colonizing at the open ends of the cut portion of the stems and block the channels through which water enters and reach the flower. This results in shortening of the vase life of cut flowers. In this regard, use of suitable low cost nanoparticles of appropriate size and quantity as antibacterial agents can become a stepping stone for overcoming post-harvest losses in the field of floriculture industry. Cut flowers of *Gerbera* species of same colour, size and batch were treated with nanoparticles

MOLTEN SALT SYNTHESIS AND PHOTOLUMINESCENCE PROPERTIES OF V_2O_5 DOPED MULLITE ($Al_{4.8}Si_{1.2}O_{9.6}$) NANOWHISKERS

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Alumina rich mullite nanowhisker of stoichiometric formula $Al_2(Al_{2.8}Si_{1.2})O_{9.6}$ was prepared by V_2O_5 doped molten salt synthesis method using Na_2SO_4 flux as molten salt media. Al_2SO_4-Na_2SO_4 system was mechanochemically activated followed by the anisotropic growth of mullite grains at relatively lower sintering temperature of 1000°C in the molten flux. The melting behaviour of the precursor composite was investigated by differential thermal analysis. The nanocrystalline mullite was characterised by X-ray diffraction, Fourier transform infrared spectroscopy and field emission scanning electron microscopy. The average diameter of the mullite particles were ~90 nm as obtained from scanning electron micrographs. Strong PL bands were observed at 311, 347, 436 and 460 nm for alumina rich mullite nanowhiskers with weak bands reflecting at 362, 379, 407 and 424 nm and the luminescene also reflected in the fluorescence microscopic images. The PL emissions for the mullite nanowhiskers are expected to result from the radioactive recombination of photo-excited holes with electrons occupying the oxygen vacancies. This Al-rich mullite nanowhiskers synthesized via molten flux, thus can be a promising material for optical applications owing to its prominent PL emission.

FABRICATION OF A SINGLE BIMOLECULAR INCLUSION COMPLEX WITH β-CYCLODEXTRIN TO IMPROVE EFFICACY OF COMBINATION DOSAGE FORM

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Introduction of multimolecules in a single inclusion complex, albeit cheaper, lacks attempt in earlier drug delivery reports.This study encompasses the first attempt to adopt a cheaper technology for incorporation ofanticancer drug combinationGefetinib and Simvastatin, in a single inclusion complex.β-Cyclodextrin (βCD) guided target inclusion complex was accomplishedby co-solvent evaporation technique. The drugs exhibit bonding interactions with the βCD through ether linkage between Gefetinib and βCD together with Simvastatin carbonyl group with βCD. Docking studies revealed that molecular alignment into βCD central cavity is achieved *via* hydrogen bonding between certain groups of the drug molecules and the polar heads of the polymer.Afterwards, the *in-vitro* dissolution study revealed that more than threefold increase in drug release from the complex in comparison to the raw drug mixture which was attributed to the complex formation inside βCD, micronization of drug and amorphous state formation of the drug particles. The kinetic modelling of the release showed zero order kinetics together with Korsmeyer-Peppas type of release profile. In addition, a low coefficient for the Korsmeyer-Peppas model was estimated suggesting slow steady release of the drugs into the solution.

SYNTHESIS OF 5-AMINO ISOCARBOSTYRIL AS A KEY INTERMEDIATE OF 5-(N-*p*CARBOXY PHENYL) AMINO ISOQUINOLINE 1,3,4-TRIONE: A NOVEL CASPASE 3 INHIBITOR

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Caspase 3 inhibitors are promising choices of drugs for apoptosis inhibitory compounds, however cytotoxicity has been of its major side effects. Thus investigation for caspase-3 inhibitor is still under search. With a view to that in this study, we have tried to design a new apoptosis inhibitory compound *in silico*, taking isoquinoline 1,3,4 trione as template. By molecular docking study and combinatorial library screening, we have found 5-(N-*p* carboxy phenyl) amino Isoquinoline 1,3,4-trione be the most potent compound in the series. The compound revealed a binding affinity -9.3 Kcal/mol. Receptor binding analysis revealed that the binding interactions between the compound and the receptor predominantly follow electrostatic and vander Waals interaction. Especially the target compound exhibited hydrogen bonding interactions with Tyr 197 and Gly125 equivalent to the standard isoquinoline 1,3,4 trione suggesting similar binding site for both the compounds. However, the target compound revealed more hydrogen bondings with the aforementioned residues due to the presence of *p*-carboxyl terminal attached with 5-NH- moiety on the main ring structure. Considering this as a promising lead, we synthesized the 5-amino Isocarbostyril as the key intermediate of the target compound. The synthesis was started by synthesizing 5-isoquinoline N-oxide from isoquinoline followed by nitration of the compound. The nitro derivative of the compound was finally reduced to amine.