Perspective on Chemist's Tool Box Towards Synthesis of Anti-tubercular Agents

Prof. Anamik Shah, Vice Chancellor, Gujarat Vidyapith, Ahmedabad – 380014.

Resurgence of Tuberculosis, especially drug resistance by Mycobacterium Tuberculosis has posed a great threat to mankind& it is now at ever alarming stage. There is a need for working on new drug discovery by more innovative ways in compare to efforts done is past. Identification of now leads and drugs is a herculean task. The present talk will give an overview of two decade of a collaborative work done by our research team involving design, synthesis, biological screening, use of bioinformatic tools & redesigning of some potential lead to arrive at some promising patented molecules.

Visualizing the structures of biological macromolecules

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Awareness of the existence of a vast microbial world inaccessible to our naked eyes but of crucial importance for our health had to await development of optical microscopes. Optical microscopes, however powerful, cannot reveal structures smaller than the wavelength of light used for imaging. Even the largest of biomolecules are much smaller than the wavelength of visible light that ranges between 400 nm and 800 nm. About a hundred years ago, X-ray diffraction, the phenomenon of scattering of X-radiation is specific directions by crystallize substances, was shown to have the power of revealing the atomic structure of molecules constituting the crystal. Over the century, the technique was developed into a powerful tool to visualize the structure of small organic molecules as well as large biomolecules. This field has revolutionized our understanding of chemistry and biology by allowing us to determine the atomic structure of hundreds of thousands of molecules. However, the technique needs crystals of the material or molecule whose structure needs to be determined. It cannot be applied to molecules in solution. Another method that has become recently available is cryo-electron microscopy. In 1924, the French physicist de Broglie suggested that electrons, till then considered as particles circling atomic nuclei, could also possess wave like properties. The wavelength associated with electrons depends on their momentum (or velocity). Ruska and Knowl succeeded in constructing the first microscope that used electron waves in 1932. In the electron microscope, electro magnets act as lenses and bend or focus the electron waves. In the "negative staining technique" of viewing biological molecules by electron microscopy, the sample is dehydrated (dried) and stained with a heavy atom salt. This distorts the molecule constituting the sample and limits the resolution of the images. To keep the samples hydrated and preserve the native structure of biomolecules, cryo-electron microscopy that operates in the temperature range of -130 to -180° C was developed. The images recorded in the microscope represent two dimensional projections. Methods were developed to obtain three-dimensional structural information using two dimensional projections. With these developments, cryo-electron microscopy has become an extremely powerful tool for studying biomolecular structure and function. The lecture will present these two techniques and their enormous impact on modern biology.

PERSPECTIVES AND CHALLENGES IN DRUG RESEARCH

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Nitrogen heterocycles are constituted a major class of existing drugs. These compounds are widely distributed in nature and are essential to life process.They also play a vital role in the controlling the metabolism of all living cells. The activity of these molecules is attributed to their ability to interfere against several important biological target sites. Keeping in view importance of nitrogen hetrocycles in antiparasitic area, we have synthesized novel heterocycles. These heterocycles were synthesized by classical solution phase as well as on solid support. Several synthesized compounds have shown promising *in vitro* and *in vivo*antiparasitic activity against Malaria and Leshimaniaparasites.The design, synthesis and antiparasitic activity of these novel antiparasitic agents will be discussed

Designing of templates to reach the distal C–H bond

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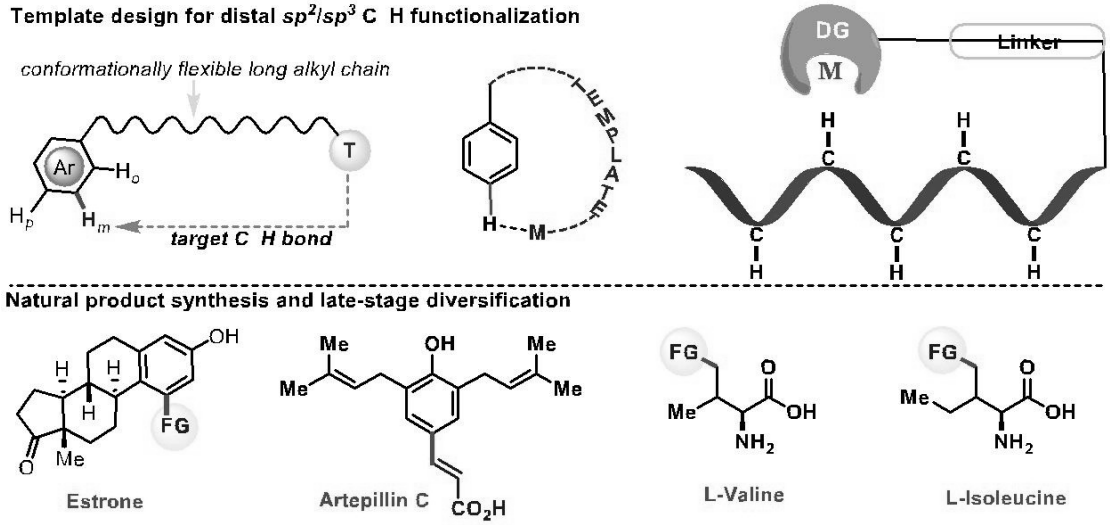
Abstract:

Mimicking the nature has always been a coveted target for scientific communinities. A precise understanding has emerged as to how enzymes accomplish the chemical transformations. Enzymes catalyze inert C-H bond functionalization in a regio- and stereoselctive manner using metal-active site. Inspired by the nature, we have developed catalytic methods to functionalize carbon–hydrogen (C–H) bonds which provides significant economic and environmental benefits over traditional synthetic methods. Applicability of our strategies towards synthesis of various complex molecules will be discussed.



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“Role of metal ions in Mycobacterial DNA damage response”

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One of the major challenges being faced in the control of TB is the increased advent of multidrug resistant forms of the pathogen. Usually the treatment of TB is prolonged since the pathogen enters into a latent state protected by a structure known as the granuloma. Within the granuloma the pathogen encounters a hostile environment rendering it prone to DNA damage. In MTB, SOS response is one of the essential systematic mechanisms against stress.

During stress conditions, the levels of metal ions concentration within the cell is altered and suggested to be have role in stress response. However, the exact roles for the metal ions are not yet clear in MTB SOS response.

Metal ions are known to stabilize, destabilize, or modulate biological molecules by introducing conformational changes and by creating centers of activity in the biomacromolecule. The distribution of these metals in the cell as a function of time and location is critical for the regulation of various biological processes. Here we will be presenting two unreported roles for metal ions in proteins that participate in mycobacterial DNA damage response.

Chemo-Catalytic Avenues for Bio-Refinery Applications

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Crude oil which is a diminishing feed stock has been the source of fuel and synthetic materials of the modern society. A step forward towards achieving sustainability and reduction in carbon footprints is the realization of Biorefinery concept, using renewable biomass feedstock for producing biofuels and chemicals. Such conversions are aimed at producing the high-value products which enhance profitability and in some cases, offer an incentive for fuel production. Biorefining is still largely unexplored territory and presents unique challenges as the bioderived molecules invariably contain more than one oxygen atom. This basic difference from the fossil derived hydrocarbons, demands design of appropriate catalysts with mostly multifunctional sites for efficiently carrying out the cascade type reactions in a single pot. Another interesting feature of bio-derived substrates is that these are multi product reactions (MPR). Hence integration of catalyst design with the optimization of process conditions makes it possible to achieve the desired product distribution. Among various bio-feedstock options, co-generated glycerol in biodiesel production and abundantly available lignocellulosic material at lower cost can be easily converted to a variety of starting materials.

This talk will cover highlights of our recent work on heterogeneous catalysts development for (i) bio-glycerol hydrogenolysis to C3/ C2 diols and propanol all of which are commercially important. (ii) carbonylation of bio-glycerol with urea to give glycerol carbonate while the transesterification with DMC to give another high value product, glycidol (iii) downstream processing of cellulose derived levulinic acid (LA) to produce γ- valerolactone (GVL) (iv) furfural is also a versatile carbohydrate derived starting material for either direct hydrogenation to give a variety of useful products such as furfuryl alcohol (FAL), tetrahydrofurfuryl alcohol (THFAL), 2-methylfuran (2-MF) and 2-methyl tetrahydrofuran (2-MTHF) or via catalytic alcoholysis (esters of LA) / hydrogenation sequence to give GVL (v)self etherification and reductive cascade etherification of 5-(hydroxy methyl) furfural (5-HMF) to cetane enhancers. All these products have extensive applications as green solvents, fuel additives and as monomers for a variety of polymeric products. The underlying basic aspect of structure-activity relation required for catalyst design will also be discussed.

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Translating Research on endophytic fungi into pharmaceutical and food Application

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Endophytic fungi are defined as fungi that live asymptomatically within the tissue of higher plants. These fungi came to limelight after the discovery of Taxol and Taxane from an endophytic fungi *Taxomycesandreanae*, of Pacific yew. Later on, a large number of bioactive metabolites from endophytic fungi have been isolated from endophytic fungi from tropical countries. Still, there is a great opportunity to discover unexplored fungi with industrial potential. There is a need to discover these fungi from less explored ecosystems e.g. cold desert, hot desert, Antartica, mangroves along with other sources like likens, bryophytes, orchids. Some of the strategies of cultivation of these fungi to stimulate the production of secondary metabolites under laboratory conditions are needed to explore the diversity of bioactive compounds. These strategies include variations in media composition, pH, temperature, aeration, or shape of culturing flask; biotic elicitation by co-culture of different strains; abiotic elicitation by physical or chemical stresses; and epigenetic modulation by chemical epigenetic modifiers. These fungi are also known to produce antioxidants, food colors and enzymes. Some of the work done in pharmaceutical and food industries and its aspect of translation of endophytic fungi research into industrial applications will be discussed.

Total Synthesis Driven Methodologies

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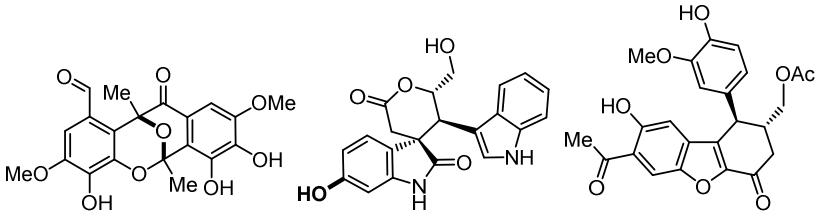
The structural complexity and skeletal diversity of natural products have served as inspirations to organic chemists for the discovery and design of new synthetic methods *en route* to their chemical synthesis. Our group focuses on the development of new methodologies that are specifically designed in the context a total synthesis of natural products of biological relevance. In this presentation, we wish to provide a comprehensive compilation of various novel transformations that have been developed in our group along with some salient aspects of the accomplished total synthesis.



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Advances in Systematics , Applications and Conservation of Fungi

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Fungi exhibits amazing diversity behave as both friends and foes. Many fungi are beneficial to human, plants, animal and environmental health. In contrast many of them are harmful and act as pathogen causing diseases. Identification and characterization of fungi is the cornerstone of many applied disciplines. Review reveals the devastating effects of some fungi which has changed the world. On the other hand it has been relized that fungal biodiversity in general can play an important role in generating bio-economy by exploring genetic and biochemical diversity captured in natural resources and maintains them in a pure state in germplasm bank and their authentication is a very important and strategic requirement for developing innovative biotechnology processes and products. The basic approaches used in detecting organism mostly rely on microscopic, cultural and morphological traits, require extensive time, labour and through classical taxonomy knowledge. In addition, subject matter specialist practicing in fungal identification is required for delivering effective results. Due to the limitations in conventional methods, and plasticity in many morphological traits of fungi, new molecular techniques developed and introduced from time to time for the investigation and rectification of identification and classification problems. A high level of molecular methods is increasingly becoming valuable tools in all aspects of fungal diagnostics, biodiversity analysis and various applications. Due to these advances global dimensions of fungi have changed tremendously and have opened improved prospects for basic and applied researches.

The current trends are towards exploring a wide diversity of fungal cultures for applied research, and it is becoming increasingly difficult to define and delimit which groups of fungi are important for technological developments. Fungi, as a whole being principal source of bioactive metabolites have established their credentials over the years as promising goldmines for a variety of bioactive metabolites and enzymes. Several economically important fungal genera which impacts our lives are being re-investigated taxonomically and systematically, like *Aspergillus*, *Penicillium*, *Colletotrichum, Cercospora*, etc. for better understanding of their biodiversity, biology, and biotechnological applications.

Among genera being reinvestigated, *Fusarium* is another important one. They survive in most soil; arctic, tropical, desert, cultivated and non-cultivated field. Due to their potent pathogenic behaviour they make their worldwide presence and cause a range of diseases leading huge losses. About 300 records of different species and *forma specialis* belonging to more than 40 different species of *Fusarium* reported from various hosts/substrates in India. About 150 isolates from diverse substrates and geographic locations in India were studied in detail at NFCCI. A glimpse of the new generic/species concept and highlights of the status of research and development of *Fusarium* and in India shall be discussed during conference.

Saroglitazar - - A CMC (Chemistry,Manufacturing and Control) Perspective

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The CMC perspectives of **First New Drug** designed, discovered, developed and launched by an Indian Pharma company, **ZydusCadila**, Ahmedabad, will be described. **Saroglitazar**was launched in Sept.2013 in India as **Lipaglyn**, for the treatment of diabetic dyslipidemia. Its chemistry, synthesis, manufacturing, impurities, IP issues, polymorphs and a broad overview of how impurities are formed, during development stage, will be discussed. The importance of understanding acid, base, oxidation, reduction, organometallic, catalytic, thermal, photochemical, stereochemical, dissolution and analytical aspects of API's and Intermediates, for predicting probable impurities, involving 8 reactive species of carbon and 5 reactive species of nitrogen, will be discussed.

Metabolic engineering facilitates developing designer bacteria for improving human health and plant growth.

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Genetic engineering facilitated exploiting a few bacteria for producing antibiotics, vitamins, many organic molecules and proteins (enzymes). However, expanding knowledge of biochemical, molecular biology and genetic manipulation aspects of a variety of bacteria enabled to design diverse bacteria for the benefit of human health and agriculture. Metabolic disorders have been increasing at an alarming rate in humans due to a variety of nutritional abnormalities and environmental toxicants. Probiotic bacteria are gaining prominent role in ameliorating these problems. Our genetic and metabolic engineering approaches enabled to transform probiotic bacteria to convert sugars into prebiotics, ameliorate the toxic effects of carcinogens, heavy metals and arsenate in rat experiments. On the other hand, metabolic engineering of rhizobacteriaviz*Pseudomonas*, *Herbaspirillum* and *Enterobacter* enabled secretion of gluconic, 2-ketogluconic, oxalic and citric acids transforming them into effective phosphate biofertilizers.

Oral Presentation

Synthesis and Biological Evaluation of Diversely Substituted Chroman Derivatives ViaUgi Reaction

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Abstract: An efficient protocol for the synthesis of diversely substituted chroman derivatives has been developed by multi component Ugi reaction. A catalytically free, simple and covineant reaction conditions were established. In order to develop better reaction condition, the reaction was carried out at different optimized conditions. The synthesized compounds are well characterized by known spectroscopic technique and were subjected to antitubercular screening.

Keyword: Chroman,Efficient protocol, Ugi reaction, Antitubercular screening.

Oral Presentation

Elucidating the metabolic basis of cancer using yeast as a surrogate: A model for tumorigenesis

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Tumor cells distinguish from normal cells by fermenting glucose to lactate in presence of sufficient oxygen and functional mitochondria, a phenomenon referred to as Warburg effect. Crabtree effect was invoked to explain the biochemical basis of Warburg effect by suggesting that excess glucose suppresses mitochondrial respiration. Ithas been known for long that yeast *Saccharomyces cerevisiae* display Warburg effect and Crabtree effect during growth on abundant glucose. Beyond this similarity, it was also demonstrated that expression of human pro-apoptotic proteins like Bax and p53 in *S. cerevisiae*leads to apoptosis. Here, we demonstrate that p53 expression in *S. cerevisiae* (Crabtree positive yeast) causes apoptosis and increase in ROS levels when cells are growing on non-fermentable carbon source like glycerol but not on fermentable carbon source like sucrose, a feature similar to tumor cells. In contrast, in *Kluyveromyceslactis*(Crabtree negative yeast) p53 causes apoptosis and increase in ROS levels regardless of the carbon source. Interestingly, the increased ROS levels and apoptosis are correlated to increased oxygen uptake in both *S. cerevisiae* and *K. lactis.* Based on these results, we suggest that at least in yeast, fermentation *per se*is not a prerequisite for escape from apoptosis. Rather Crabtree effect plays a crucial role in determining whether the cells should undergo apoptosis or not.

Oral Presentation

A novel salt-tolerant rhizospheric*Bacillus safensis*S8, improves growth of pearl millet under saline condition

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ABSTRACT

Aim: Development of an effective plant growth promoting rhizobacteria (PGPR) inoculant necessitates a diverse set of traits that can help its colonization in the rhizosphere and survival under varying environmental conditions. **Methods:** The PGP ability of the bacterial isolate S8 was evaluating for biofertilisation (phosphate solubilization and ammonia production), biostimulation [indole acetic acid (IAA) production] and bio-control (HCN production, hydrolytic enzyme production and antagonistic effects) activities. The efficacy in augmenting salt tolerance in pearl millet under NaCl stress (0mM, 100 mM, 200mM). **Results:** Isolate S5from the rhizosphere of pearl millet grew at up to 15% NaCl (w/v) and displayed specific PGPR traits, such as the production of IAA, siderophore, ammonia, HCN, P-solubilisation, hydrolytic enzyme production and their bio-control efficiency. Characterization of this isolate using polyphasic approaches involving both phenotypic and genotypic attributes led to its identification and designation as *Bacillus safensis*S8**.** **Conclusion:***Bacillus safensis*S8 appears as effective PGPR inoculants as it possesses a number of traits useful in establishment and proliferation in saline regions. Further studies on its pot trail applications are in progress.

Acknowledgments

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Oral Presentation

Biodegradation of Textile dye Effluent using Bioreactors – Tactics of Immobilization of Laccases

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Rhizopusoryzae and a purified laccase from this organism were able to degrade triarylmethane, indigoid, azo, and anthraquinonic dyes and textile dye effluent that contained these dyes. Initial decolorization, degradation and detoxification velocities depended on the substituents on the phenolic rings of the dyes. Immobilization of *Rhizopusoryzae* laccase on Scotch Brite enhanced the thermal stabilities of the enzyme and its tolerance against some enzyme inhibitors, such as halides, copper chelators, and dyeing additives. Treatment of effluent with the immobilized laccase almost reduced their toxicities. Detoxification reaches to almost 98% and there was undocked biodegradation and decolorization that would be blossoming in environmental pollution. A new era towards Green Revolution.

Oral Presentation

Analytical Method Development and Validation of Pharmaceutical Products ---- A Triumph for Synthetic Drugs

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The development of sound Analytical method is of supreme importance during the process of drug discovery, release to market and development, culminating in a marketing approval. The main objective is to review the method development, optimize and validation of the method for the drug product which is API from the developmental stage of the formulation to commercial batch of the product. Method development for the interested component in finished product or in process tests and the sample preparation of drug product and to provide practical approaches for determining selectivity, specificity, limit of detection, limit of quantitation, linearity, range accuracy, precision, recovery solution stability, ruggedness, and robustness of liquid chromatographic methods by UPLC to support the Routine, in process and stability analysis. The positive result would be the capstone of success.

Oral Presentation

Production and Charcterization of Pigments Produced By EpicoccumPurpurasense MTCC 9351

Adarsh Kumar Singh[a,b], Dr.Neeta Raj [a,b]

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ABSTRACT

Colour is a vital constituent and is probably one of the first characteristics perceived by the senses. In food industry various synthetic colours are used and these colour are very harmful for human beings, so with the increasing awareness of toxicity of synthetic colours, demand for pigments from natural sources has increased in now days. Natural coloursare generally extracted from fruits, vegetables, roots and microorganisms and are often called "biocolours" because of their biological origin. Various synthetic colouring agents have the potential of carcinogenicity and teratogenicity. So many microorganisms like Monascuspurpureus, Penicillium sp. ,Epicoccumetc can be explored to produce pigments in suitable conditions.

Keywords- Epicoccum, Biocolours, synthetic colours,pigments,microorganisms

Oral Presentation

Development of Deuterium Labeled Pharmaceutically Active Compounds

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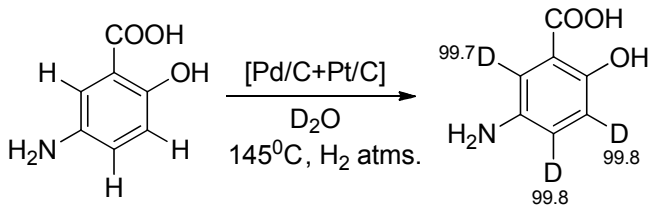
Key Words: Mixed catalyst, Deuteration, Mesalamine, C-H activation, Deuterated drugs

Abstract: A convenient and efficient lab-scale protocol for stable deuteration of Mesalamine, with mixed catalyst 10% Pt/C (25 wt%) and 10% Pd/C (10 wt%) at 145°C, using D_2O as deuterium source, in hydrogen atmosphere, is reported.The nature of reactive species with Pd/C–Pt/C–D2O–H2 system issuggested to be of electrophilic nature D^+type.



Oral Presentation

Stimulation of the growth of *Vignaradiata* under saline condition by the plant growth promoting bacterium *Bacillus* sp.M124

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ABSTRACT

Aim: Plant growth promoting rhizobacteria (PGPR) enhance the plant growth by direct and indirect mechanisms and enhance the growth productivity of agricultural crop in saline condition. **Methods:***Bacillus* sp. M124 isolated from the rhizospheric soil of pearl millet from Morbi district, Gujarat, India.This study was carried out to evaluate the efficacy of isolate M124 for indol-3-acetic acid (IAA) production, phosphate solubilization, ammonia production and secretion of hydrolytic enzyme. The isolate was then used as an inoculant for the vegetative study of *V. radiata* plant with different treatment of NaCl concentration. **Results:** Isolate M124from the rhizosphere of pearl millet grew at up to 15% NaCl (w/v) and displayed studied hydrolytic enzyme production and showed varied level of IAA production at different time interval. It also able to solubilize phosphate. The isolates also enhance the growth of *V. radiate* in presence of saline condition. **Conclusion**: The results validate the *Bacillus* sp. M124 could be use in production of plant growth promoting effect for agricultural crops for development of eco-friendly sustainable agriculture.

Keywords:*Bacillus* sp., salt tolerant, Phyto-hormones, hydrolytic enzyme production, ammonia production, seed germination, phosphate solubilization

Acknowledgments

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Multi-trait plant growth promoting (PGP) rhizospheric bacteria isolated from medicinal plant *Leucasalba*

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Abstract

Aim: in recent years, pathogenic attacks are one of the major threats to the growth and productivity of crop plants. Currently, instead of use of synthetic fungicides, the plant growth promoting bacteria has been considered eco-friendly in nature. Against, soil saline environment root associated beneficial bacteria can help improve plant growth and nutrition. **Methods:** four salt tolerant PGPR strains were isolated from rhizosphere of *Leucas alba* from saurashtra university, Rajkot, Gujarat, India. All the PGPR strains were able to show growth at up 5% NaCl (w/v). The isolation was done in four different media (NA, KB, Jenson's Media, ASM agar). Phosphate solubilization, ammonia, and IAA secretion of rhizospheric strain was tested. Moreover, bio-control (hydrolytic enzyme production and antagonistic effects) activity also measured. **Results:** SULA 7 showed highest percentage inhibition against *Rhizoctonia*sp. All isolates showed varied level of IAA, ammonia production at different time intervals. **Conclusions:** PGPR strains isolated under present investigation may be useful as a novel biofertilizers for crop production at saline region. Further studies on its biochemical and molecular identification are in progress.

Keywords: Rhizospheric bacteria; Antifungal production; Agricultural applications, IAA

Acknowledgments

The Authors are thankful to the DST- Science and Engineering Research Board (SERB), New Delhi, India for providing financial support under National Postdoctoral Fellowship (NPDF) scheme (File No. PDF/2015/000430/LS, 06 June, 2016) as well as Prof. RK Kothari, Head & Co-ordinator of Institute of Biotechnology for providing excellent research laboratory facility.

COMPARATIVE ASSESSMENT OF ANTIOXIDANT ACTIVITY AND PHYTOCHEMICAL ANALYSIS OF TWO PLANTS PEELS BELONGS TO RUTACEAE FAMILY USING DIFFERENT EXTRACTION TECHNIQUES

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Abstract

This study was designed to evaluate the antioxidant activity of two plants peels of Rutaceae family. The extraction was done by individual cold percolation (Petroleum ether, acetone, methanol, aqueous), Infusion, maceration (methanolic&ethanolic), decoction, ultrasonication and microwave assistant extraction methods. The antioxidant activity was evaluated using antioxidant assay, 2, 2-diphenyl-1-picryl hydrazyl free radical scavenging assay. Total phenol and flavonoid content was also measured. The antioxidant activities showed different levels in different extracts. This suggests that significantly influences the choice of solvent and methods for extraction. This study demonstrated that peels of both plants, could serve as good source of antioxidants for use in the preparation of dietary supplements or nutraceuticals, food ingredients, pharmaceutical, and cosmetic products.

The life change is possible without altering DNA

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Abstract

Revolution of life through the belief. The implications of this research radically change our understanding of life. It shows that not only genes and DNA control our biology; that instead DNA is controlled by signals from outside the cell, including the energetic messages emanating from our positive and negative thoughts. In this era quantum biology is being hailed as a major breakthrough showing that our bodies can be changed as we retrain our thinking.

While the eukaryotic genome is the same throughout all somatic cells in multicellular organism, there are specific structures and functions that discern one type of cell from another. These differences are due to differential gene regulation during developmental stage as well as healthy and diseases condition. Interestingly, these cell-specific gene expression patterns can be affected by an organism's environment throughout its lifetime leading to phenotypical changes that have the potential of altering risk of some diseases. Both cell-specific gene expression signatures and environment mediated changes in expression patterns can be explained by a complex network of modifications to the DNA, histone proteins and degree of DNA packaging called epigenetic marks. Several areas of research have formed to study these epigenetic modifications, including DNA methylation, histone modifications, chromatin remodeling and microRNA (miRNA).

Keywords: The belief, control internal environment through positivity, Epigenetics, gene expression pattern change by mi RNA as well as modification of histone and DNA.

A convenient and facile Synthesis of Coumarino Imidazole derivative - An approach towards Green Chemistry

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In present world process chemistry has a noteworthy importance. To improve pathway by undergoing less steps, and less consumption of energy and solvent free reactions by carrying out various trials. Coumarin and imidazole moiety being of vital pharmacological importance, the present work is related to fuse the imidazole ring at 3,4 position of the coumarin. Work includes a facile and convenient and solvent free reductive cyclization of imidazole ring on the coumarin ring. The aim of the studies was to develop a product by different pathway and high yield. The entire synthesized compounds were confirmed different spectroscopic techniques such as NMR, Mass, IR and Elemental analysis

ISOLATION AND SCREENING OF LACTIC ACID PRODUCING BACTERIA FOR BIOTECHNOLOGICAL PURPOSE

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ABSTRACT

Lactic acid bacteria is group of gram positive organism which have the property of converting lactose and other sugars to lactic acid through fermentation of carbohydrates. Lactic acid bacteria produce organic acid mainly lactic acid which have ability to inhibit the growth of many especially pathogenic gram negative bacteria, so whey water the translucent liquid rich in lactose, vitamin, protein obtain as by product after precipitation of curd used as the starter medium for lactic acid bacteria for lactic acid production.

The main aim of this work was to study the fermentation of whey for the production of lactic acid. The effect of different process parameters such as temperature, inoculums size, incubation time and pH of the medium is carry out to check the conversion of whey sugar to lactic acid.

x

Synthesis and antimicrobial evaluation of some new 1,3,4- oxadiazoles

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ABSTRACT:
Recently the investigations in the field of oxadiazole have intensified due to the large number of uses of oxadiazoles in the most diverse areas, 1,3,4- oxadiazole derivatives have been reported to show biological activities like bactericideand fungicideproperties. These observations and our previous workof oxadiazole prompted us to synthesize unreported derivatives of 1,3,4- oxadiazole. A series of 2-((4-acetyl-5-(aryl)-5-methyl-4,5-dihydro-1,3,4-oxadiazol-2-yl)methylthio)-3-o-tolylquinazolin-4(3H)-one was synthesized by the cyclization of imines using acetic anhydride. The Schiff base are obtained by the reaction of appropriate carbonyl compound with 2-(4-oxo-3-o-tolyl-3,4-dihydroquinazolin-2-ylthio) acetohydrazide. The structure of synthesized compounds was characterized by IR, ^{1}H-NMR, ^{13}C-NMR and mass spectrometry. The synthesized compounds were screened for their antimicrobial activity against different strains of Gram-negative (*E. coli* and *P. aeruginosa*) and Gram-positive (*S. aureus* and *S. pyogenus*) bacteria and selected fungi *C. albicans, A. niger*and *A. clavatus* using serial broth dilution method. Our approach is to focus on the modification of synthetic pathway for the said reaction with respect to time and other physico-chemical parameters.

"Stem Cells" – A Therapeutic Boon , No Science Fiction Anymore

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Stem cells are an unspecialized cells having the capacity for self-renewal and capability of proliferation and differentiation to various cell lineages. Stem cells have the remarkable potential to develop into many different cell types in the body during early life and growth. In addition, in many tissues they serve as a sort of internal repair system, dividing essentially without limit to replenish other cells as long as the person or animal is still alive. They are vital to the development, growth, maintenance, and repair of our brains, bones, muscles, nerves, blood, skin, and other organs. They can be classified into embryonic stem cells (ESC) and non-embryonic stem cells (non-ESC). Regenerative medicine, the most recent and emerging branch of medical science, deals with functional recovery of tissues or organs for the patient suffering from severe injuries or chronic disease. The spectacular progress in the field of stem cell research has laid the foundation for cell based therapies of disease which cannot be cured by conventional medicines. Advancements in gene editing and tissue engineering technology have endorsed the ex vivo remodelling of stem cells grown into 3D organoids and tissue structures for personalized applications. This Brief review elucidate the tremendous potential of stem cells in Therapeutics and Clinical Medicine.

Key Words: Stem cells, Regenerative medicine, Therapeutics, Therapy.

Citric acid production from pineapple waste by *Aspergillus niger*

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Abstract

A Submerged fermentation used for citric acid productionfrom pineapple waste by *Aspergillus niger*. The media was supplemented with glucose, sucrose, ammonium nitrate, ammonium phosphate,coppersulphate and clacium chloride with optimum pH. It was found that pineapple waste with sucrose and ammonium nitrate gave the optimum citric acid when fermented for 5 days at optimum temprature with optimum moisture content.Theyeild was based on the amount of fermentable sugerconsumed.The results present the use of pineapple waste as a cheap medium for the production of citric acid by *Aspergillus niger*.

Potential application of *Bacillus subtilis* lipopeptides in toothpaste formulation.

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ABSTRACT

Biotoothpaste is the toothpaste that contains biologically active ingredient. Toothpaste contains sodium lauryl sulfate (sls) as an anionic surfactant, emulsifier and cleaning agent. In the present work *Bacillus subtilis* was used as a source for the production of bio surfactant (lipopeptides) or emulsifiers. After 2 days of production period bio surfactant was extracted using acid alkali precipitation method. And finally obtained powdered bio surfactant was used along with the other ingredients for the formation of bio toothpaste. The physicochemical properties were analyzed considering several tests mainly spreading ability, water activity, pH, foaming and cleaning tests. The obtained results indicated that the bio surfactant was as efficient as the chemical surfactant confirming its potential utilization in toothpaste formulation compared to the commercial one. The evaluation of the antimicrobial activity was detected. The results showed that the biotoothpaste exhibited an important antimicrobial activity.

Defective Green Coffee Beans as Nutrient Source for Pesticide Degrading Bacteria

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Abstract

Generally glucose, peptone, meat and beef extract used as primary substrates in the study of pollutant cometabolism. In the presence of more favorable carbon sources can inhibit the degradation of xenobiotics so sometimes primary substrates fails. To overcome this problem, natural wastes maybe used. Defective green coffee brand may be great source as primary substrate. Green coffee beans has a great chemical and biological complexity, and it used as co-substrate to remove toxic recalcitrant pollutants. From this defective green coffee beans, four bacteria strains were isolated. This four bacterial strains are capable to grow and remove DDT [1,1,1-trichloro-2,2-bis (4-chlorophenyl) ethane] and PNCB [1-CHLORO-4-NITROBENZENE] in a liquid medium. Result showed that defective green coffee beans was an ample nutrient source for bacterial growth and it significantly enhanced DDT and PNCB biodegradation in comparison with glucose.

Isolation and screening of Polyhydroxyalkanoates producing halophilic bacteria from mangrove soli sample

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• Abstractः

Polyhydroxyalkanoates (PHAs) are storage materials that accumulate by various bacteria as energy and carbon reserve materials. They are biodegradable, environmentally friendly, and biocompatible bioplastics. Unlike petrochemical-based plastics that take several decades to fully degrade, PHAs can be completely degraded within a year by variety of microorganisms into CO2 and water. In this study, I isolate mangrove soil sample from konkan coast, Arabian sea (dumas beach) Were collected for the isolation of microorganism. Which are responsible to production of PHA. Those strain are inoculated in to E_2 mineral medium for several days at 37°c with rotary shaker at 180 rpm, after 30 h withdraw sample for cell dry weight(CDW) and PHA content analysis, and we can also check the effect of N_aCL concentration, PH, and nitrogen source on growth of PHA producing bacteria.

The objective of the present work is to isolate halophilic bacteria from mangrove soil samples and screen the bacterial isolates for their ability to utilize carbon source to produce PHA.

Role of Chitosan in Encapsulation of Nanofertilizer to Enhance Production in Agriculture

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Abstract

Nanotechnology is the the art and science of building stuff that does stuff at the nanometer scale. Nanotechnology (sometimes shortened to "nanotech") is the study of manipulating matter on an atomic and molecular scale. Generally, nanotechnology deals with structures and sized between 1 to 100 nanometers in at least one dimension, and involves developing materials or devices within that size.

Nowadays nanofertilizers are taking special attention in agriculture research for better growth and productivity. Nanoferlizers are the fertilizers works at nanoscale synthesized using nanotechnology. They are important tools in agriculture to improve crop growth, yield and quality parameters with increase nutrient use efficiency, reduce wastage of fertilizers and cost of cultivation. Nanofertilizers provide more surface area for different metabolic reactions in the plant which increase rate of photosynthesis and produce more dry matter and yield of the crop.

Chitosan is a biopolymer, a chitin derivative, a compound which is completely safe for the environment. Due to its polymeric cationic, biodegradable, bioabsorbable and bactericidal characteristics, chitosan (CS) nanoparticle is an interesting material for use in controlled release systems. Chitosan is obtained as a result of chemical or enzymatic chitin deacetylation

The encapsulated fertilizers, in which fertilizers are entrapped within nanoparticles and protect it for better survival in inoculated soils, allowing for their controlled release into the soil. The method of encapsulation of fertilizers components in polymeric, chitosan nanoparticle is relatively novel with potential commercial applications. Accelerating plant growth and productivity through the application of nanofertilizers can open new perspectives in agricultural practices, because nanofertilizers promise to be a safe way to enrich nutrients to plants without doing harm to the environment.

EFFECT OF CHLORPYRIPHOS DEGRADATION BY JR16NUTRITIONAL AND ENVIRONMENTAL PARAMETERS ON

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Abstract:

Chlorpyriphos is a member of the organophosphate class of insecticides. This class has become one of the most widely used groups of pest control chemicals. In 1989 nearly 40% of the $6.2 billion global insecticide market was comprised of organophosphates (OPs). Chlorpyriphos is registered for use in nearly 100 countries and is annualy applied to approx 8.5 millions crop acres. CPP is used to kill number of pests including insects and worms. Effect of several nutritional and environmental parameters was checked on chlorpyriphos degradation by JR16. The optimum conditions were observed to be 20 h old inoculum, 5% inoculum size, static culture conditions, 28°C temperature and pH 7.0. The maximum growth was observed in sucrose as carbon source and yeast extract as nitrogen source in chlorpyriphos containing Bushnell Hass medium.

Keyword: Organophosphate, Chlorpyriphos, Optimization, Degradation

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Effect of ACC-deaminase producing Bacillus cereus on the growth of *Vignaradiata* (Mung beans) under salinity stress

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Abstract :

Bacillus cereus isolated from the rhizosphere of *Brassica nigra* growing in the saline desert of Radhanpur (India), was identified on the basis of biochemical and 16S rDNA analysis. Salinity stress induces higher levels of ethylene in plants which limits crop production. This increased concentration of ethylene can be reduced by using plant growth promoting rhizobacteria (PGPR) producing ACC-deaminase. *Bacillus cereus* produces ACC deaminase (0.22 U.ml-1), siderophore (85% U), IAA (3.36 µg.ml-1) and solubilizes phosphate (150 µg.ml-1). *B. cereus* has the ability to grow over pH 5-11 and in the presence of up to15% NaCl. Talc-based *B. cereus* formulation (2×10 8 cfu.g-1) was prepared and evaluated for its plant growth promoting activity. Root elongation of *Vignaradiata* in salt stress conditions (1.2 S.m-1) was 3.6 cm while in control it was 2.5 cm. The results show that salinity stress decreased mung bean growth significantly but inoculation of *B. cereus* reduced the inhibitory influence of salt stress on mung bean growth.

Histological studies of Leaf Regenerated Cultures of Biodiesel Crop (*Jatropha curcas* L.)

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Abstract:

*Jatropha curcas*has attracted the attention of scientists and entrepreneurs equally as a natural source of biodiesel. The plant being wild in nature, has erratic behaviour in seed yield production. Therefore, few elite plants were selected on the basis of consistant yield behaviour and oil content for mass propagation through tissue culture. Attempts were also made to regenerate the plants through direct organogenesis. Here we reports histology of leaf regenerated cultures showing direct organogenesis rather than callus formation. Histological sections (6µM) prepared during culture initiations suggest that leaf as explants can be used for direct organ formation so as to reduce the time period taken for generating the plantlets indirectly via Callus formation. We also did comparative studies of *In vitro* and *In vivo* cultures of *J.curcas* through scanning electron microscopy (SEM). Major differences were observed in midrib hairy structure and leaf stomata.

Topic: Isolation and Screening of Cellulase Producing Bacteria using Fruit Peels

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Abstract:

The present work has been undertaken for the isolation of cellulose producing bacteria and to detect unit activity of cellulase by using fruit peel as a substrate. Cellulase producing microorganism are most important in textile and paper industries. Soil sample from farmland were used for the isolation of cellulase producing bacteria. Bacterial colonies were screened for cellulase production on Carboxy Methyl Cellulose agar plate and zone of CMC utilization was detected using iodine solution. The unit enzyme activity was measured by DNSA method. Remarkable production of cellulase was achieved by 2.5% pineapple peel at 37^0C temperature.

Isolation and Screening of Cellulase producing Bacteria using Fruit peels

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Abstract

Aim of present investigation was to isolate the Cellulase producing Bacteria and to detect the unit activity of Cellulase by using fruit peels as substrate. Cellulase producing Microorganisms are most important in industries with large application in textile industries and paper industries. Soil samples from farm land were used for isolation of cellulase producing bacteria. Bacterial colonies were screened for cellulase production on the CMC agar plate & zone of CMC utilization was detected by using iodine solution. The unit enzyme activity was measured by DNSA method. Remarkable production of Cellulase was achieved by 2.5% pineapple fruit peels at 37°C temperature.

Key Words: Cellulase, Fruit peels, DNSA.

Assessment of medicinal phytochemical extracts for their Quorum inhibitory potential against *Pseudomonas aeruginosa* and *Erwiniacarotovora*

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Quorum sensing(QS) is a density dependent bacterial cell–cell communication process that involves the production, detection, and response to extracellular signaling molecules known as autoinducers. QS systems are ubiquitous in bacteria, and have since been found to regulate diverse cellular functions including luminescence, biofilm formation, antibiotic production, virulence factor expression, pigment production, plant-microbe interactions, mating and motility. *Pseudomonas aeruginosa* is a nosocomial pathogen responsible for fatal pulmonary infections, urinary tract infections and surgical site infections in immunocompromised individuals. *Erwiniacaratovora*causes soft rot and blackleg in potato tubers which leads to great loss to agricultural commodities. Pathogenic attributes and virulence factors of these pathogens are under control of QS. The compounds that inhibit cell-to-cell communication in prokaryotes, known as Quorum sensing inhibitors(QSIs) has offered a novel method of pathogen management in animals and plants. QSIs have been reported from algae and plant. However, Indian medicinal plants have not been explored much. The present study explores the potential of Indian medicinal plants as a source for promising QSIs against pathogenic bacteria.

Keywords: *Quorum sensing, Autoinducers, Phytochemistry, Extraction, Pathogenesis*

ONE-POT SEQUENTIAL APPROACH FOR THE CONSTRUCTION OF HIGHLY FUNCTIONALIZED TRIAZOLO[4,3-c]PYRIMIDINES.

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Abstract:

Novel 1,2,4-triazolo[4,3-c]pyrimidine-8-carboxamides were synthesized via oxidative cyclization of hydrazono-1,6-dihydropyrimidine-5-carboxamide intermediates by the application of iodobenzenediacetate as a sole cyclizing agent. Here, we report a one-pot sequential strategy to generate the corresponding triazolopyrimidines by condensation of prepreparedacylketenedithioacetals and arylamidines. Moreover, this process describes the application of presynthesizedarylamidines, which omits the Suzuki-Miyaura cross-coupling reaction and hence provides metal-free organic synthesis in an atom and step economical fashion.

Synthesis and antitumor activity of highly functionalized indole derivatives

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Abstract

We have successfully applied bioisoster approach for the design and synthesis of new anticancer molecules from β-carboline motif. The newly synthesized molecules were tested for their in vitro anticancer activity against various cancer cell growths. The most active compounds from the newly synthesized derivatives were tested for their in vivo as well as primary mechanistic study. We found that, these derivatives exhibits potent antitumor activity against CCRF-CEM, PC3, H1299 & OECM1 solid tumour growths. The most potent derivatives were further screened for in vivo study using xenograft model. Primary mechanistic study revealed that they exhibit anticancer effect through DNA cross linking & Topoisomerase inhibition.

Synthesis and anticancer activity of nitrogen mustard derivatives

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Abstract

In the current project, we have synthesized a series of new water soluble N-mustard-benzene conjugates (I, Fig. 1) prepared by linking phenyl N-mustard pharmacophore with benzene moiety through a urea linker. This series of compounds were prepared via structure modifications of **Compound-A**, previously synthesized in our laboratory, by bioisostere approach. The benzene ring bears a variety of ω-N,N-dialkylaminoalkylamide or ω-cyclicaminoalkyl amide side-chains located to the meta- or para-position of the urea linker. The tertiary amino function on the side-chain can be converted into a variety of water-soluble salts with various acids. The newly synthesized derivatives were subjected to evaluate for their antitumor activities both in vitro and in tumor xenograft model. The results showed that the newly synthesized conjugates were also found to have a broad spectrum of antitumor activity against a panel of human leukemia and solid tumor cell growth in culture. Among these derivatives, compound **Compound-9b** and **Compound-9a** were selected for further antitumor studies. It was revealed the **Compound-9b** is more cytotoxic than **Compound-A**in inhibiting cell growth of various tumor cell growth in vitro. It also showed that this agent is more potent than **Compound-A** against human colon HCT-116, prostate PC3, and lung cancer H460 xenografts in mice with less toxicity. Studies on the mechanism of action revealed that **Compound-9b** is able to induce DNA cross-linking and cell arrest at G2/M phase. The present investigations conclude that **Compound-9b** has high potential to be selected as a candidate for preclinical antitumor studies.

A validated stability indicating chromatographic method for the simultaneous estimation of Camylofin with NSAID drugs and a new approach of method transfer from classical HPLC to a modern UPLC instrument

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ABSTRACT

The presented work describes the method development of simultaneous determination of Camylofindihydrochloride (CMF), Diclofenac potassium (DCF) and Paracetamol (PCM) using reversed phase high performance liquid chromatography (HPLC- UV) and the method was further transfer to a new generation instrument; ultra performance liquid chromatography (UPLC- PDA).The detailed validation carried out for the combination tablet formulation of CMF and DCF by UPLC- PDA. From the method development study, Acquity UPLC HSS C18 (2.1×50mm, 1.8µm) was finally selected for validation. The satisfactory results observed for peak shape, retention time and resolution with a mobile phase of 20mM ammonium acetate buffer (pH 3.0 with dilute ortho phosphoric acid): methanol (33:67v/v). The elution of mobile phase was maintained at a flow rate of 0.250ml/min; isocratically and detection was carried out at 220nm. Both of drugs were efficiently separated out in less than 3.5min with 1.1 and 3.2 min of retention time of the CMF and DCF with 11.87 of resolution. The linearity was obtained in the 20.0-80.0µg/ml range of concentration with 0.9998 of correlation coefficients for the substances. The method was analyzed for specificity; with detailed force degradation study; which is a simple, precise and accurate method, as per the International Conference on Harmonization (ICH) guidelines.

Production of amylase using Banana waste by *Bacilius subtilis*

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ABSTRACT:

Amylase is one of the most important and of great significance . Amylase could be potentially useful in the pharmaceutical, fine chemical industries of enzymes, medicinal and analytical chemistry and other application. Amylase can be derived from several sources ,such as plants, animals and microorganisms. Banana waste was used as a substrate for the production of amylase by *Bacillus subtilis* using solid state fermentation. First *Bacillus Subtilis* was grown on nutrient broth. Then, this active culture was used as inoculum in the production medium of amylase. Then substrate Banana peel was added to the medium . After 24 hours Amylase was extracted and Bioassay of amylase was performed. The various parameter were optimized the incubation period, substrate concentration, pH and incubation temprature.

Microwave Assisted Cu(I)-CatalyzedHighly Efficient Approach for One-Pot Synthesis of Pyrazole Derivatives Using A^3 Coupling.

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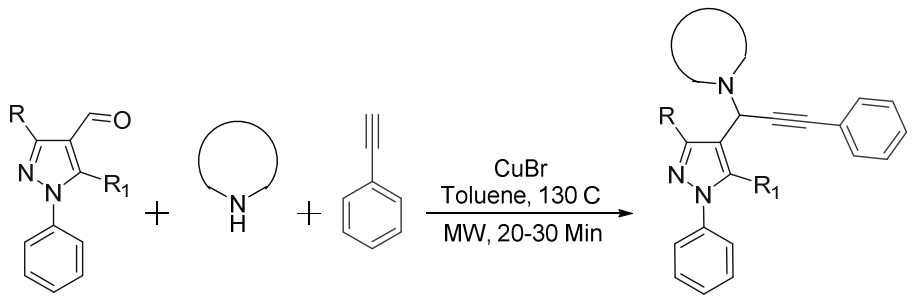
Abstract:

CuBr-catalyzed three component one-pot A3 coupling reactions were investigated under microwave irradiation.Although metal-catalyzed A3-coupling reactions have been extensively used to synthesize various propargylamine. Till A3 coupling is not tested in many heterocycles like substituted pyrazole.Pyrazole-4-carboxaldehydes, alkynes and amines with a variety of structures have been tested against Copper based catalyst. Best results achieved by Copper(I)bromide catalyst via microwave irradiation. Overall 15 subtracts of Pyrazole based propargylamine was synthesize . A catalyst loading of 20 mol% was sufficient to give excellent yields under microwave irradiation. In this study, set of reactions carried out under various Cu (I) and Cu (II) catalysts as well as different solvents and different stoichiometric ratio. This synthesis route made a great difference and resultant protocol was very convenient and excellent yielding for the generation of a broad substrateof heterocyclic substituted propargylamine.

Graphical Abstract:



Keywords: Pyrazole-4-carboxaldehydes, A3 coupling, Copper Catalyzed, Microwave Assisted

Potassium *tert*-Butoxide Catalyzed Three Component Domino Reaction Strategy: Synthesis of Triazolo[5,1-b]quinazoline and Benzimidazo[2,1-b]quinazoline Derivatives.

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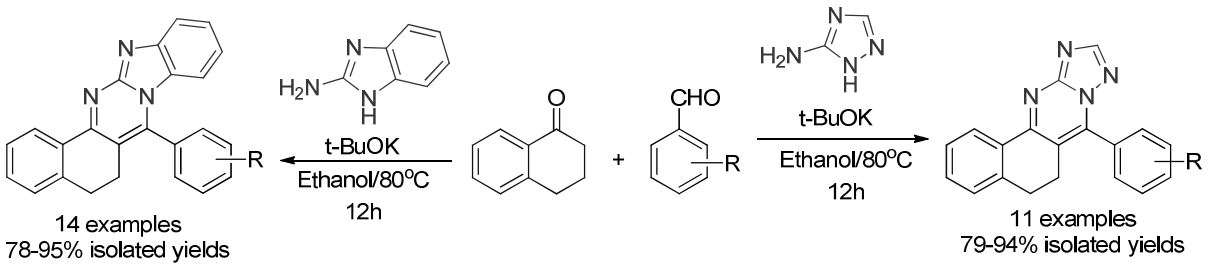
Abstract: Three-component reactions of α–tetralone with 1,2,4-triazol-5-amine/2-aminobenzimidazole and aromatic aldehydes have been discovered by using potassium *tert*-butoxide (*t*-BuOK) as a catalyst. A series of new and polyfunctionalized triazolo[5,1-*b*]quinazolines and benzimidazo[2,1-*b*] quinazolines were synthesized. The significant advantages of the developed strategy involve the construction of the corresponding heterocycles by eliminating the use of precious catalysts under a mild condition in good yields.

Graphical Abstract:



Keywords:2-Aminobenzimidazole, Benzimidazo[2,1-b]quinazoline, Domino reaction, Potassium tert-butoxide, α–Tetralone, 1,2,4-Triazol-5-amine, Triazolo[5,1-b]quinazoline.

"Multi component approach toward pyrazolo[1,5-a]pyrimidine; Design, synthesis and characteristics studies"

Prakash L. Kalavadiya[1] and Hitendra S. Joshi[2*]
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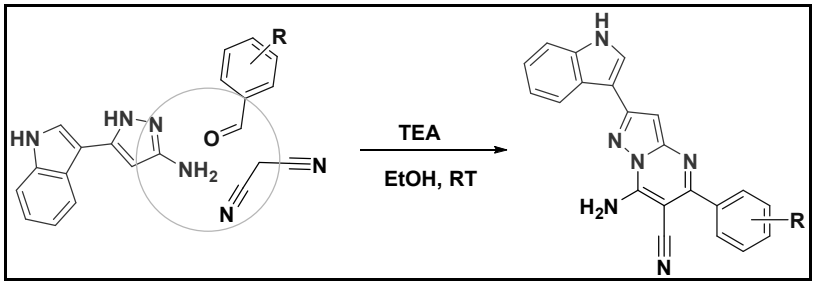
Abstract:

Nitrogen-containing heterocyclic compound great interest since they exhibit numerous biological activities. In present work, we have synthesisindole-basedpyrazolo[1,5-a]pyrimidin derivative viathree component one port reaction of 5-(1H-indol-3-yl)-1H-pyrazol-3-aminewith malononitrile and various aromatic aldehyde. The significant advantage of the developed strategy involves mild basic, environmentally friendly condition and having a good yield at room temperature.

All the synthesized compounds are characterized by using various spectroscopic techniques like ^{1}H-NMR, ^{13}C-NMR, Mass and IR spectroscopy.



Keyword: pyrazolo[1,5-a]pyrimidin, three component one port condensation,mild basic condition, room temperature, domino reaction.

Reference:

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Novel indolizino[8,7-b]indole hybrids as anti-small cell lung cancer agents: Regioselective modulation of topoisomerase II inhibitory and DNA crosslinking activities.

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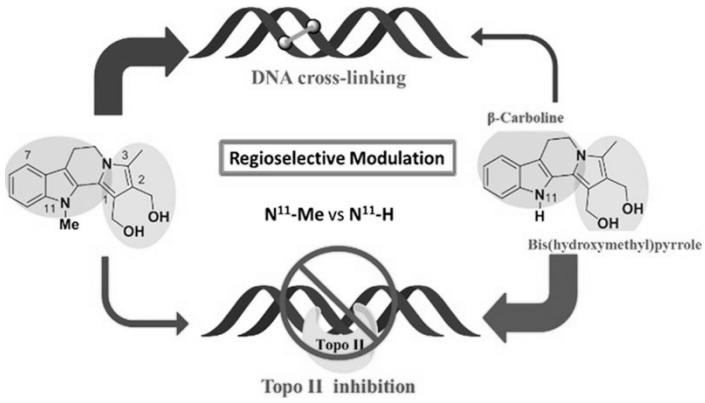
Abstract::A novel series of bis(hydroxymethyl)indolizino[8,7-b]indole hybrids composed of b-carboline (topoisomerase I/II inhibition) and bis(hydroxymethyl)pyrrole (DNA cross-linking) are synthesized for antitumor evaluation. Of tumor cell lines tested, small cell lung cancer (SCLC) cell lines are the most sensitive to the newly synthesized compounds. These hybrids induce cell cycle arrest at the G2/M phase, trigger tumor cell apoptotic death, and display diverse mechanisms of action involving topoisomerase II (Topo II) inhibition and induction of DNA cross-linking. Intriguingly, the substituent at N11 (H or Me) plays a critical role in modulating Topo II inhibition and DNA cross-linking activities. N11-Me derivatives predispose to induce DNA crosslinks, whereas N11-H derivatives potently inhibit Topo II. Computational analysis implicates that N11-Me restrict the torsion angles of the two adjacent OH on pyrrole resulting in a favorable of DNA cross-linking. Among these hybrids, compound 17a with N11-H is more effective than cisplatin and etoposide, but as potent as irinotecan, against the growth of SCLC H526 cells in xenograft model.

Graphical abstract:



Keywords:Anti-SCLC hybrids, b-carboline, bis(hydroxymethyl)pyrrole, indolizino[8,7-b]indole, DNA cross-linking Topoisomerase inhibition