In order of Importance, list of 10 best papers of the applicant highlighting the important discoveries/contributions described in them briefly

TOPICAL DELIVERY OF DRUGS

OCULAR APPLICATION (SOLID DOSAGE FORM):

1. **1. Development and characterization of nano-fiber patch for the treatment of glaucoma, T Garg, B Malik, G Rath, AK Goyal, European Journal of Pharmaceutical Sciences 2014, 53, 10-16**
   (Impact Factor: 3.616, Citation Index: 112)

In the present work polymeric nano-fiber patches was developed for the effective treatment of glaucoma using timolol maleate and dorzolamide hydrochloride as model drugs. The nano-fibers were prepared by electrospinning technique and were characterized on the basis of fiber diameter, morphology, entrapment efficiency, mucoadhesive strength, and drug release behavior, etc. Final formulations were inserted in the cul-de-sac of glaucoma induced rabbits and the efficacy of the formulation was evaluated. The results clearly indicated the potential of the developed formulation for occur drug delivery. There was a significant fall in the intraocular pressure compared to commercial eye drops.

2. **Development of nanofibrous ocular insert for retinal delivery of fluocinolone acetonide, J Singla, T Bajaj, AK Goyal, G Rath, Current eye research, 2019, 44 (5), 541-550**
   (Impact Factor:1.693, Citation Index: 10)

Topical formulations are less effective in treating retinal inflammatory diseases due to poor avaliability of drug at target tissues. Nanofibers due to their unique structural features show great promise for drug delivery to retinal segment following topical application. The aim of the present study was to design preservative free controlled release ocular drug delivery system for improved drug availability at the target site with higher patient compliance. The fluocinolone acetonide-loaded PCL nanofibers were prepared by electrospinning technique. Optimized formulation was chosen on the basis of outcome of inclusive in-vitro characterization, SEM, FTIR, XRD, in-vitro release, isotonicity, sterility, and biodegradibility. The relative efficacy of optimized formulation was investigated in rabbits against its marketed counterpart. The prepared fibers were sterile, smooth, non-woven and they showed extended drug release behavior. Ocular and plasma kinetics showed therapeutic levels at the target site while minimizing systemic distribution. Preclinical results established that PCL nanofibers serve as a promising drug carrier for retinal segment.

WOUND HEALING APPLICATION:

3. **Collagen nanofiber containing silver nanoparticles for improved wound-healing applications, G Rath, T Hussain, G Chauhan, T Garg, AK Goyal, Journal of drug targeting, 2016, 24 (6), 520-529, 112**
   (Impact Factor:3.38, Citation Index: 112)

Electrospun nanofibers showing great promise for fabricating nanostructured materials might help to improve the quality of wound care. The present study aimed to investigate the wound-healing potential of collagen nanofiber mats containing silver nanoparticles. Silver nanoparticles (AgNPs) synthesized by the chemical reduction method were incorporated in collagen nanofibers during the electrospinning process. Characterization of electrospun nanofiber mats revealed a mean fiber diameters in the range of 300-700 nm with a sustained release of silver ions shown to follow pseudo-order kinetics. MIC of AgNPs against Staphylococcus aureus and Pseudomonas aeruginosa were evaluated using micro-dilution assay and further antimicrobial activity of fabricated nanofibers was performed. Finally, in vivo studies were performed to demonstrate the wound-healing efficacy of composite nanofibers. In vitro results confirmed the potential antimicrobial efficacy provided by AgNPs and AgNPs composite nanofibers, essential to provide an aseptic environment at the wound site. In vivo study revealed that the rate of wound healing of the composite nanofiber mats was found to be accelerated compared with plain collagen nanofibers. Histology analysis revealed an accelerated re-epithelization, collagen production, and better wound contraction with AgNPs composite collagen nanofibers.

4. **Development and characterization of cefazolin loaded zinc oxide nanoparticles composite gelatin nanofiber mats for postoperative surgical wounds, G Rath, T Hussain, G Chauhan, T Garg, AK Goyal, Materials Science and Engineering: C 58, 242-253.**

(Impact Factor: 7.328, Citation Index: 84)

Systemic antibiotic therapy in post-operative wound care remain controversial leading to escalation in levels of multi-resistant bacteria with unwanted morbidity and mortality. Recently zinc (Zn) because of multiple biophysiological functions, gain considerable interest for wound care. Based on our current understanding, the present study was designed with an intent to produce improve therapeutic approaches for post-operative wound management using composite multi-functional antibiotic carrier. The study involved the fabrication, characterization and pre-clinical evaluation of cefazolin nanofiber mats loaded with zinc oxide (ZnO) and comparing co-formulated mats with individual component, enable a side by side comparison of the benefits of our intervention. Minimum inhibitory concentration (MIC) of the drug, ZnO nanoparticles (ZnONPs) and drug-ZnONP mixture against Staphylococcus aureus was determined using micro dilution assay. The fabricated nanofibers were then evaluated for in-vitro antimicrobial activity and the mechanism of inhibition was predicted by scanning electron microscopy (SEM). Further these nanofiber mats were evaluated in-vivo for wound healing efficacy in Wistar rats. Study revealed that the average diameter of the nanofibers is around 200-900 nm with high entrapment efficiency and display sustained drug release behavior. The combination of ZnO and cefazolin in 1:1 weight ratio showed

higher anti-bacterial activity of 1.9 ± 0.2 µg/ml. Transmission electron microscopy of bacterial cells taken from the zone of inhibition revealed the phenomenon of cell lysis in tested combination related to cell wall disruption. Further composite medicated nanofiber mats showed an accelerated wound healing as compared to plain cefazolin and ZnONP loaded mats. Macroscopical and histological evaluations demonstrated that ZnONP hybrid cefazolin nanofiber showed enhanced cell adhesion, epithelial migration, leading to faster and more efficient collagen synthesis. Hence the fabricated composite nanofiber mats have the potential to be used as a postoperative antimicrobial wound dressings.

MICROBICIDAL FORMULATIONS

5. **Development and characterization of niosomal gel for topical delivery of benzoyl peroxide, G Goyal, T Garg, B Malik, G Chauhan, G Rath, AK Goyal, Drug delivery 22 (8), 1027-1042.**
(Impact Factor:6.419, Citation Index: 100)

Benzoyl peroxide (BPO) is generally considered as first line treatment against acne. Low water solubility and formation of larger clusters and limited skin permeation upon topical application necessitates the application of high amount of drug for desired action which leads to induction of skin irritation. In the present study, we developed BPO-loaded niosomal formulation to improve its permeation through skin. The niosomes were further loaded in the carbopol gel to improve contact time. The results of the skin permeation study, skin retention study revealed that niosomes can effectively improve the drug permeation through skin. Application of niosomal gel significantly reduced the bacterial load after a treatment of four days. This reduction in bacterial load was further resulted in a significant reduction in the inflammation with minimal skin irritation compared with plain drug and the plain niosomal formulation.

6. **(Copper–curcumin) β-cyclodextrin vaginal gel: delivering a novel metal–herbal approach for the development of topical contraception prophylaxis, C Gaurav, R Goutam, KN Rohan, KT Sweta, CS Abhay, GK Amit, European Journal of Pharmaceutical Sciences 65, 183-191**
(Impact Factor:3.616, Citation Index: 21)

Delivering a safe and effective topical vaginal contraceptive is the need of present era. We explored the potential of a metal (copper) and herbal moiety (curcumin) for this topical contraceptive prophylaxis. Complex of copper and curcumin (Cu-Cur) was synthesized and the concerns regarding its aqueous solubility was resolved by including it into the hydrophobic cavity of β-cyclodextrin (β-CD) as (Cu-Cur)CD inclusion complex. Dose assessment was made on the basis of in-vitro spermicidal assays and cell cytotoxicity studies. Finally the (Cu-Cur)CD loaded vaginal gel was prepared, characterized and evaluated for in-vitro spermicidal activity and preclinical toxicity studies. Spectral and morphological characterizations confirmed the synthesis of (Cu-

Cur) and (Cu-Cur)CD inclusion complex. Spermicidal assays and Hela cell cytotoxic data revealed an optimized 1.5% (Cu-Cur)CD for further studies. 1.5% w/w (Cu-Cur)CD loaded carbopol 974p gel provided 100% motility even at 2-fold dilution and preclinical toxicity studies in Rats and Rabbits revealed its highly safe profile. The hypothesis of considering metal-herbal complex and its cyclodextrin complex has worked and the well planned strategy of including it in (β-CD) cavity provided a preeminent platform for vaginal delivery. In-vitro assays and preclinical toxicity analysis confirmed its potential to be used as highly safe and effective prophylaxis.

7. **Albumin stabilized silver nanoparticles–clotrimazole β-cyclodextrin hybrid nanocomposite for enriched anti-fungal activity in normal and drug resistant Candida cells, C Gaurav, G Nikhil, S Deepti, S Kalra, R Goutam, GK Amit, RSC advances, 2015, 5 (87), 71190-71202**

(Impact Factor:3.119, Citation Index: 18)

Nanotechnology unlocked distinctive platforms to move inside a hybrid therapeutic zone. Currently, nano-metal technology is the targeted field with exceptional advantages. Exceptionally small size and dominance of the surface properties such as high surface charge has raised a great deal of interest. This work is designed to exploit an interesting mechanistic feature *i.e.* multiple therapeutic targets possessed by metal nanoparticles. In this study we selected silver nanoparticles (AgNPs), which possess well documented anti-fungal activity and a standard antifungal molecule *i.e.* "clotrimazole". A hybrid of AgNPs and clotrimazole was aimed to tackle clotrimazole resistance. Clotrimazole was firstly included into a β-cyclodextrin cavity to render it water soluble; subsequently the drug loaded dextrin moiety is functionalized on the surface of bovine serum albumin (BSA) stabilized silver nanoparticles using 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide/*N*-hydroxysulfosuccinimide (EDC/ NHS) chemistry. BSA stabilisation was essential to shield the physical interaction of AgNPs with the clotrimazole β-cyclodextrin complex that is otherwise experienced. Spectral and morphological characterization of the complex assures the synthesis of a hybrid metal complex. A cellular toxicity assay was performed to determine the toxic nature of the hybrid. This hybrid was then evaluated for its fungicidal activity on normal and clotrimazole resistant *Candida* cells. The toxicity and efficacy outcomes revealed a potent profile with a handy therapeutic window. Mechanistic explanations for this hybrid nature were supported by aggravated apoptotic cell percentage and reactive oxygen species production in both resistant and non-resistant cells. Cell cycle arrest studies further revealed G_2/M phase cell cycle arrest, directing towards compromised cell membrane and DNA synthesis process equivalently in clotrimazole resistant cells.

8. **In-vitro anti-viral screening and cytotoxicity evaluation of copper-curcumin complex, G Chauhan, G Rath, AK Goyal, Artificial cells, nanomedicine, and biotechnology, 2013, 41 (4), 276-281**

(Impact Factor:3.343, Citation Index: 18)

Multiple therapeutic activities attributed to curcumin deliver a challenge to explore its hidden qualities. Structural features set an opportunity to chelate metal ions and enhance the therapeutics in a specified direction. A metallo-herbal complex (MHco) of

curcumin with copper (Cu(2+)) ions was synthesized and characterized by various spectroscopy techniques. It was screened for its antiviral activity and cytotoxicity. Studies revealed that the synthesized compound has good microbicidal activity and would be utilized for the development of vaginal microbicidal gel against viral infections.

9. **Development and characterization of nanocarriers for topical treatment of psoriasis by using combination therapy, N Parnami, T Garg, G Rath, AK Goyal, Artificial cells, nanomedicine, and biotechnology 42 (6), 406-412**

(Impact Factor:3.343, Citation Index: 66)

Psoriasis is an autoimmune, chronic, inflammatory skin disease characterized by epidermal hyperplasia, proliferation of blood vessels, and infiltration of leukocytes in dermis and epidermis. Several immunosuppressants such as methotrexate (MXT) and cyclosporine are used but they are associated with adverse effects due to down regulation of immune system. Numerous approaches have been explored to overcome the problems of conventional topical system such as high frequency of application, impermeability to skin barrier, and limited efficacy. Photodynamic therapy is another non-invasive technique currently used for skin diseases. The combination of two drugs is also commonly observed to achieve more effective therapy. In the present study, antipsoriatic activity of niosomal formulations for the treatment of psoriasis in combination with narrow and broad band UV radiation had been explored in experimental animal model.

10. **Electrospun composite nanofiber-based transmucosal patch for anti-diabetic drug delivery, A Sharma, A Gupta, G Rath, A Goyal, RB Mathur, SR Dhakate, Journal of Materials Chemistry B 1 (27), 3410-3418**

(Impact Factor: 6.331, Citation Index: 75)

The intention of the present investigation was to develop an oral formulation for an anti-diabetic drug that not only could deliver it in the active form but also provide a sustained and controlled release profile. A biodegradable poly(vinyl alcohol) (PVA) and sodium alginate (NaAlg) electrospun composite nanofiber based transmucosal patch was developed and the anti-diabetic drug insulin was loaded in it by active loading. The drug entrapment in the composite nanofibers during the processing was confirmed by scanning electron microscopy, atomic force microscopy, X-ray diffraction and Fourier transform infrared spectroscopy. The *in vivo* studies were carried on male Wistar rats by the sublingual route. The mucoadhesive strength results confirmed that the drug loaded PVA–NaAlg nanofiber patch had the highest strength among the PVA, PVA–NaAlg and drug loaded PVA–NaAlg samples, due to its higher water holding capacity. The *in vitro* activity provided a sustained and controlled release pattern of the drug from the nanofiber patch. *In vivo* activity validated the fact that insulin was delivered in its active state and showed appreciable results when compared to the commercial formulation. The insulin release follows first order kinetics followed by an initial burst release necessary to produce the desired therapeutic activity. Furthermore an encapsulation efficacy of 99% of

the experimental formulation provides sufficient indication that the composite nanofibers serve as an ideal carrier for the delivery of insulin *via* the sublingual route. Thus the present investigation gives impetus to work in the direction of delivering anti-diabetic drugs (proteins and peptides) *via* the oral route using electrospun composite nanofiber transmucosal patches.