Current Trends in **Pharmaceutical Research** 2018, 5(2):15-17
ISSN 2310-4820

www.dibru.ac.in/ctpr

EFFECT OF HPMCK15M AS GELLING AGENT ON DRUG RELEASE KINETICS FROM OLEOHYDROGEL HYBRID

Dipanjana Ash*, Shubham Mukherjee, Sutapa Biswas Majee and Gopa Roy Biswas
Dept. of Pharmacy, NSHM Knowledge Campus, Kolkata -Group of Institutions
124, BL Saha Road, Kolkata 700053, India

Abstract:

Background: "Oleohydrogel hybrid" is a combination of two different components, the oleogel phase formed by apolar lipophilic phase consisting of soybean oil and non-ionic surfactants and hydrogel component consisting of gelling agent in aqueous base [1]. The hybrid possesses the characteristics and benefits of both the phases [2].

Objective: The main aim of the present investigation was to determine the effect of HMPCK15M as a gelling agent in the hydrogel component on release kinetics of paracetamol from the oleohydrogel hybrid system.

Methods: Two formulations of 2% w/w paracetamol containing soybean oil-based oleohydrogel hybrid were prepared by mixing oleogel (25 % w/w of Span 40: Tween [2:1]) with 1.5% (OH 1) and 3% (OH2) HPMCK15M hydrogels. The formulations were characterised by FTIR, extrudibility, spreadability, drug release kinetics in phosphate buffer (pH 5.8) and hemocompatibility. The models selected included zero order, first order, Higuchi and Korsmeyer Peppas model.

Results and discussion: FTIR study indicated compatibility between the components of the oleohydrogel hybrid. The hybrids demonstrated good extrudibility and spreadability (Table 1). Drug release studies on OH 1 and OH 2 revealed 43.82% and 37.63% release in 7 h. respectively (Fig 1). Both formulations revealed time dependent release kinetics (Table 2). Low percentage of drug release from OH2 might be due to higher viscosity. Moreover, it exhibited zero order kinetics in first 3 hrs due to swelling-controlled drug release but followed first order kinetics in last 4hrs. Probably complete swelling of the hydrogel component of OH2 led to rapid drug release by Fickian diffusion. For OH 1, lower viscosity resulted in uniform

*E-mail: dipanjanaash16@gmail.com , Contact no: 9733820735

mixing of the oleo and hydrogel components in vitro leading to zero order kinetics with non-Fickian diffusion in last 4 hrs.

Conclusion: Therefore, percentage of HPMCK15M as gelling agent in soybean oil-based oleohydrogel hybrid produced significant effect on drug release kinetics which exhibited time-dependent pattern.

References:

1. MM Ibrahim, SA Hafez, MM Mahdy (2013). Organogels, hydrogels and bigels as transdermal delivery systems for diltiazem hydrochloride: Asian J Pharm Sci. 8:48-57.
2. VK Singh, A Anis, I Banerjee, K Pramanik, MK Bhattacharya, K Pal. (2014). Preparation and characterization of novel Carbopol based bigels for topical delivery of metronidazole for the treatment of bacterial vaginosis: Mater Sci Eng C. 44: 151-58.

Table 1: Evaluation parameters of OH 1 and OH 2

Batch	**% HPMCK 15M in hydrogel component**	**Colour**	**Odour**	**Appearance**	**pH**	**Extrudibility (cm/sec)**	**% Spreadability (using 10-100gm)**
OH 1	1.5 %	Yellowish-white	odourless	Smooth non-oily	5.5	0.95-1.0	28-80%
OH 2	3.0%	Yellowish-white	odourless	Smooth non-oily	5.5	0.9-1.0	30-86%

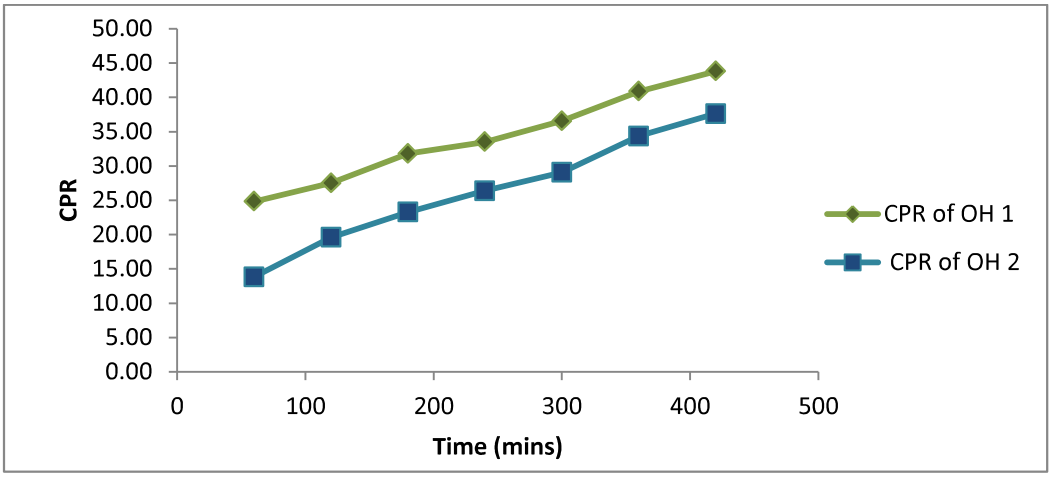

Fig 1: Release profile of OH 1 and OH 2 in phosphate buffer (pH 5.8) at 32ºC

Table 2: kinetics modelling of drug release data of OH 1 and OH 2

Batch		Zero order		First order		Higuchi	Korsmeyer Peppas
		First 3 hr	Last 4 hr	First 3 hr	Last 4 hr		
OH 1	R^2	0.9834	**0.9945**	**0.9973**	0.9657	0.9704	0.9487
	n	-	-	-	-	-	**0.291**
OH 2	R^2	**0.9936**	0.9855	0.97	**0.9902**	0.9854	0.9899
	n	-	-	-	-	-	**0.506**

Current Trends in **Pharmaceutical Research** 2018, 5(2):18
ISSN 2310-4820

www.dibru.ac.in/ctpr

NANOCOSMETICS: EFFICACY AND SAFETY ASSURANCE

Farak Ali*, Shahnaz Alom, Mohan Upadhyay, Bitopan Baishya, Bishwa Narayan Kondoli and Dibyojyoti Sarmah
Department of Pharmaceutical Sciences,Dibrugarh University, Assam-786004.

Abstract:
Nanotechnology has found widespread application across various streams of science including the field of cosmetics by taking the name of nanocosmetics. The efficacy of nanocosmetics enhances due to its nanostructure providing a great advantagesover conventional cosmetics, as it ameliorate the properties like color, permeability, transparency, solubility etc.[1]. Nanomaterials like nanoemulsions, nanosponges, dendrimers, nanosomes, nanocapsules and nanocrystals can be utilized for the development of nanocosmetics. Several nanocosmetic preparations include moisturizer, lipstick, facial mask, sunscreens, possesses some potential limitation concerning toxicity issues, technological barriers and economic aspects [2]. This limitation can be minimized by undertaking some safety assurance like *in vitro* tests for dermal complication (episkin, epiderm, NRPT), laser scanning confocal microscopy for nanoparticle toxicity and mathematical modeling [3]. The era of nanocosmetics has already started and science surrounding these nanomaterial subjects will continue to evolve with the development of new testing methods, leads to safer, healthier and beautiful future. This review reports the recent development, efficacy and safety aspects of nanocosmetics.

Keywords: *Nanotechnology, Nanocosmetics, Nanotoxicity, In vitro Test.*

References:

1. Raj S., Jose S., Sumod U. S., Sabitha M. Nanotechnology in cosmetics: Opportunities and challenges. Journal of Pharmacy and Bioallied Sciences, 2012, 4(3): 186-193.
2. Nanda S, Nanda A, Lohan S, Kaur R, Singh B. (2016). Nanocosmetics: Performance enhancement and safety assurance. 47-67. DOI: 10.1016/B978-0-323-42868-2.00003-6
3. Shokri J. Nanocosmetics: benefits and risks. Bioimpacts, 2017, 7(4): 207-208.

*E-mail: *alifarak347@gmail.com, Contact no: 7002079840*

Current Trends in **Pharmaceutical Research** 2018, 5(2):19-20
ISSN 2310-4820

www.dibru.ac.in/ctpr

A REVIEW ON REGULATORY GUIDELINES FOR NANOPHARMACEUTICALS

ManishaSahariah*,Herny Duarah*, Bonita Chetia, Chinmoyee Borah
Department of Pharmaceutical Sciences, Dibrugarh University, Dibrugarh-786004, Assam.

Abstract:

Background: Nanotechnology is an emerging branch in pharmacy and involved in the development of carrier in novel drug delivery systems(Patel & Shah, 2017). Extensive research in nanotechnology has raised its area of applications and scope to enhance bioavailability and stability of drugs. The modification and improvement of new and existing testing methods and models for evaluation of toxicity is a serious concern. Therefore,these parameters need to be addressed by formulation scientists and regulatory authorities instead of approving for human use(Sharma, 2015).

Objective: The objective of this review is to study the existingregulatory guidelines proposed and implemented by various regulatory authorities for development of safe formulations.

Methods: Considering the importance of this issue, a thorough literature survey was carried out through online databases to understand the guidelines of regulatory authorities such as FDA, EMA, MHRA, NANOREG and NNI and possibilities for implementation in pharmaceutical industry involved in production of nanopharmaceuticals.

Results and Discussion: The changesof physicochemical properties like surface charge and binding affinities due to smaller size need to be addressed. Nanopharmaceuticalshave an inadequatestandardized nomenclature. In addition, significant changes inphysicochemical characteristicsmay be considered to develop particular test methods (Hock, Ying, & Wah, 2011). In this aspect,FDA and EMA took initiative bypublishingtechnical documents to be followed by various industries associated with production of nanopharmaceuticals (Chopra &Jaggi, 2018).

Conclusion: An investigator should focus on development of safe nanopharmaceuticals to minimize the risk. The regulatory authorities should

*E-mail: *manishasaharia2@gmail.com; hernyduarah@gmail.com*

also closely monitor safety issues and accordingly, guidelines may be modified from time to time.

Keywords: EMA; FDA; MHRA; Health hazard; Nanotechnology; Toxicity.

References:

Chopra,D.S.; Jaggi, A. S. (2018). Nanopharmaceuticals: Safety and regulatory considerations. Pharma Times , 50(2), 84–86.

Hock, S. C., Ying, Y. M., & Wah, C. L. (2011). A review of the current scientific and regulatory status of nanomedicines and the challenges ahead. PDA Journal of Pharmaceutical Science and Technology, 65(2), 177–195. http://www.ncbi.nlm.nih.gov/pubmed/21502077

Patel, P., & Shah, J. (2017). Safety and Toxicological Considerations of Nanomedicines: The Future Directions. Current Clinical Pharmacology, 12(2), 73–82. https://doi.org/10.2174/1574884712666170509161252

Sharma, H. K. (2015). Risk Assessment of Nanoformulations. Recent Patents on Drug Delivery & Formulation, 9(2), 106. https://doi.org/10.2174/1872211309666150407120040

Current Trends in **Pharmaceutical Research** 2018, 5(2):21-23
ISSN 2310-4820

www.dibru.ac.in/ctpr

EVALUATION OF ANTIMICROBIAL POTENTIAL OF HERBAL HYDROGEL PREPARED WITH PURE BIOACTIVE FRACTION OF METHANOLIC LEAF EXTRACT *CASSIA ALATA.L* AGAINST SKIN DISEASES

[1]Parbin Iraqui*, [2]Tapash Chakrabarty, Malay Kumar Das and R.N.S Yadav
*[1]Department of Life Sciences, Dibrugarh University, Dibrugarh-786004
[2]Department of Pharmaceutical Sciences, Dibrugarh University, Dibrugarh-786004

Abstract:
Background: The North Eastern region of India is blessed with various medicinally important plants and herbs due to its rich biodiversity and these are used by its local people for a long time to treat diseases. (Pal, 1984, Singh et al., 1996, Shankar et al., 2012). Microbial infections are increasing day by day due to indiscriminate use of synthetic antibiotics which triggers resistance in microbes (Clark, 1996). Hence herbal medicines are gaining importance worldwide to treat these infections as these have least or no side effects. Skin infections are very much prevalent to this region because of its hot and humid climate and use synthetic drugs give adverse effect on body. Therefore herbal topical formulation can be an alternative way to treat these microbial skin infections (Khan et al., 2012).
Objectives: The objectives of the study were to develop an herbal antimicrobial hydrogel from the pure bioactive fraction of methanolic leaf extract of *Cassia alata* L. and evaluation of its pharmaceutical potential against skin diseases using wistar albino rats.
Methods: Methanolic leaf extract of *Cassia alata. L* with antimicrobial activity against *Staphylococcus aureus* (MTCC 9542) and *Candida albicans* (MTCC 4748) was subjected to column chromatography. Most potent column fraction was tested with TLC and further purified with preparative HPLC. Bioactive pure fraction was characterized with IR, LC-MS and NMR. This bioactive fraction was incorporated with gel to prepare 1% (w/w) bioactive fraction based herbal hydrogel and evaluated for its physical and rheological properties (Stulberg et al., 2002, Ramchandani, 2013). Then it was tested for its *in vitro* antimicrobial activity against *Staphylococcus*

*E-mail: parbin4msnr@yahoo.com, Contact no- 9957466711

aureus and *Candida albicans*. Its wound healing potential was evaluated in wistar albino rat model with surgical site infection in the dorsal area (Shukr and Metwally, 2013). Finally microbial bio-burden study was performed to check the effectiveness of the hydrogel in the skin tissue of the treated rats.

Result and Discussion: Column chromatography of the extract produced one highly bioactive column fraction (F12) that contains two compounds, further purified as PF1 and PF2. Out which, only one pure fraction (PF1) was found to be bioactive and characterized as aliphatic in nature having alocohol and ketone as its functional groups. Pure bioactive fraction, PF1 containing hydrogel fulfils all the physical and rheological properties of a standard gel. It gave positive results in *in vitro* antimicrobial activity against tested microorganisms. Evaluation of *in vivo* antimicrobial activity revealed that the prepared hydrogel not only showed faster wound healing in rats compared to marketed antimicrobial formulation but also gave complete healing. Microbial bio-burden study revealed that the skin tissue homogenate of hydrogel treated rat groups contain less number of bacterial and fungal cell in them than the marketed antimicrobial formulation treated groups.

Conclusion: This herbal gel significantly enhanced the wound healing as assessed by the contraction of wound length and bio burden characteristics compared to the marketed antimicrobial formulations. The formulated herbal gel could find use as very promising and innovative topical alternative for the treatment of skin infections caused by bacteria as well as fungal strains without hazard to human health based on the fact of its traditional use by the Assamese people with no toxic effects. These findings may open new avenues for the treatment of dermal infections by local application of the herbal antimicrobial gel. However, further preclinical and clinical studies are recommended to support its efficiency claims in humans. Further approaches are needed to clearly elucidate the full mechanism of action of such natural preparations in the healing of wound.

Key words: Antimicrobial, bio burden, fraction, bioactive, hydrogel.

References:

Clark A. M. Natural products as a resource for new drugs. Pharmaceutical Research. 1996; 13:1133-1144.

Khan MM, Mueen I, Muhammad AH, Shahid M M, Naqvi SA, Shahid M, Jaffar M J. Antioxidant and antipathogenic activities of citrus peel oils. J Essent Oil Bear Plant. 2012; 15:972 –979.

Mahesh K.M.V.S., Talluri V. P., Rajagopal S. V. Purification and characterization of bioactive compound from the methanolic leaf extract of *Millingtonia hortensis* Linn. Int J Pharm. 2015; 6:348–58.

Pal GD. Observation on ethnobotany of tribes of Subansiri, Arunachal Pradesh. Bull Bot Surv India 1984; 26:26-37.

Ramchandani U. Formulation and evaluation of topical gel of ketoprofen using different polymers. International Journal of Pharmaceutical & Biological Archive. 2013; 4: 323–326.

Shankar R, Deb S, Sharma BK. Antimalarial plants of Northeast India: an overview, J Ayurveda Integr Med. 2012; 3:10-16.

Shukr M. H., Metwally G. F. Evaluation of topical gel bases formulated with various essential oils for antibacterial activity against methicillin-resistant *Staphylococcus aureus*. Tropical Journal of Pharmaceutical Research. 2013; 12:877–884.

Singh J, Bhuyan TC, Ahmed A. Ethnobotanical studies on the Mishing tribes of Assam with reference to food and medicinal plants. J. Eco. Taxon Bot. 1996; 12:350-356.

Current Trends in **Pharmaceutical Research** 2018, 5(2):24-25
ISSN 2310-4820

www.dibru.ac.in/ctpr

FUTURE ASPECTS OF ANTI-DIABETIC NANO-FORMULATION FROM HERBAL SOURCE

Riya Saikia*, Kalyani Pathak and Aparoop Das
Department of Pharmaceutical sciences, Dibrugarh University, Dibrugarh 786004, Assam

Abstract:

Background: Diabetes is a chronic metabolic disorder that affects millions of people worldwide. In recent years, nanotechnology has given new hope for the formulation of effective drugs against diabetes (Grover et al., 2002) Nano phytomedicines is prepared from active phytoconstituents or standardized extracts of plants. Nano-sized drug delivery systems of herbal drugs have a potential future for enhancing the activity and overcoming problems associated with plant medicines for treatment of Diabetes (Yadav et al.,2011).

Objective: The current review focuses on Nano-formulations from herbal origin for the treatment of diabetes mellitus, a major crippling disease in the world leading to huge economic losses.

Methods: Newer nanotechnology based herbs have been developed that have efficient biopharmaceutical properties and desirable target characteristics. In phyto-formulation research, developing nano dosage forms like Polymeric Nanoparticles ie. Nanospheres and Nanocapsules, Liposomes, Proliposomes, Solid Lipid Nanoparticles [SLNs], Nanoemulsion, etc. has large number of advantages for herbal drugs, including enhancement of solubility and bioavailability, Besides the discussion has been extented to impart the basic techniques available to develop the nano-formulations from herbs (Singh et al.,2011)

Results and Discussions: Several studies and research reports based on nano technological approaches in the formulation of anti-diabetic drugs from plant source have pointed out the fact that research in the formulation of nano-drugs improved strategies for combating diabetes based on the possible molecular mechanism of action of the drugs (Patwardhan et al., 2004). Herbal mediated nano particles are having less particle size,

*E-mail: saikia.riya27@gmail.com

more surface area, more solubility which results in the optimum dose of drug that can reach to systemic circulation (Ramachandran et al., 2002).

Conclusions: Further, this review sheds light on enhancing the efficacy of herbal drugs in novel ways for successful diabetes treatment.

Key Words: Diabetes, Nanotechnology, Herbal drugs, Particle size and Solubility

References:

1. Grover, J.K., Yadav, S., and Vats, V.: Medicinal plants of India with antidiabetic potential. J. Ethnopharmacol., 81, 81–100, 2002.
2. Yadav D, Suri S, Choudhary A.A., Sikender M., Hemant, Beg N.M., et al. Novel approach: Herbal remedies and natural products in pharmaceutical science as nano drug delivery systems. Int J Pharm Tech. 2011; 3:3092–116.
3. Singh R.P., Singh S.G., Naik H, Jain D, Bisla S. Herbal excipients in novel drug delivery system. Int J Comprehensive Pharm. 2011; 2:1–7.
4. Patwardhan B, Vaidya A.D., Chorghade M. Ayurveda and natural products drug discovery. Curr Sci. 2004; 86:789.
5. Ramachandran, A., Snehalatha, C., and Viswanathan, V.: Burden of type 2 diabetes and its complications- the Indian scenario. Curr. Sci., 83, 1471–1476, 2002

Current Trends in **Pharmaceutical Research** 2018, 5(2):26-27
ISSN 2310-4820

www.dibru.ac.in/ctpr

FORMULATION VARIABLES AFFECTING DRUG RELEASE FROM BIGEL

Shubham Mukherjee*, Dipanjana Ash, Sutapa Biswas Majee, Gopa Roy Biswas
Dept. of Pharmacy, NSHM Knowledge Campus, Kolkata -Group of Institutions
124, BL Saha Road, Kolkata 700053, India

Abstract:

Background: Bigels are novel formulations composed of biphasic structured systems obtained by mixing hydrogel and oleogel. Such systems can overcome the major drawbacks of either of the single phases and possess the advantages of both [1]. Variables affecting the characteristics of bigels and drug release include concentrations of organogelators in organogel, strength of hydrogels depending on polymer molecular weight and concentration, method of drug incorporation, ratio of organogel: hydrogel etc. [2].
Objective: Bigels were prepared in the two different ratios 1:1 and 2:1 of hydrogel: oleogel. with drug incorporated in hydrogel or organogel phase. The objective of the current study was to demonstrate the effect of the formulation variables on paracetamol release form bigels.
Methods: Soyabean oil-based oleogels were prepared with 22% organogelator (Span 60). Hydrogels were obtained with 3% w/w hydroxypropyl methylcellulose. Paracetamol (2% w/w) was selected as the model drug for the study. The bigel was prepared by adding oleogel to hydrogel at two ratios. FTIR analysis, extrudibility spreadibility and drug release studies were carried out.
Results and Discussion: FTIR study confirmed chemical compatibility of the bigel components. Four bigel formulations showed good extrudability and spreadability (Table: 1). Drug release from bigel [hydrogel: oleogel (1:1)] containing drug in the hydrogel phase was found to be 56.23% in 6h. However, only 26.47% paracetamol released in 6 h from 1: 1 bigel with drug in the oleogel phase. Similarly, it was observed that 84.39% drug was released in 6h from 2:1 bigel with paracetamol added in the hydrogel phase

*E-mail: rx.shubhamm@gmail.com , Contact no: +919831730574

and it decreased to 22.60% in the 2:1 bigel where the drug was in oleogel. (Fig: 1)

Conclusion: Therefore, ratio of hydrogel:oleogel as well as method of drug incorporation in the bigel altered the percentage of drug release from the formulations.

References:

1. VY Andonova, PT Peneva, EG Apostolova and et al; Carbopol hydrogel/sorbitan monostearate-almond oil based organogel biphasic formulations: Preparation and characterization of the bigels: Tropical Journal of Pharmaceutical Research, 2017, 16 (7), 1455-1463.
2. SP Kodelaa, P Pandeya, SK Nayak and et al; Novel agar–stearyl alcohol oleogel based bigels as structured delivery vehicles: International Journal of Polymeric Materials and Polymeric Biomaterials; 2017, 66(13), 669-678.

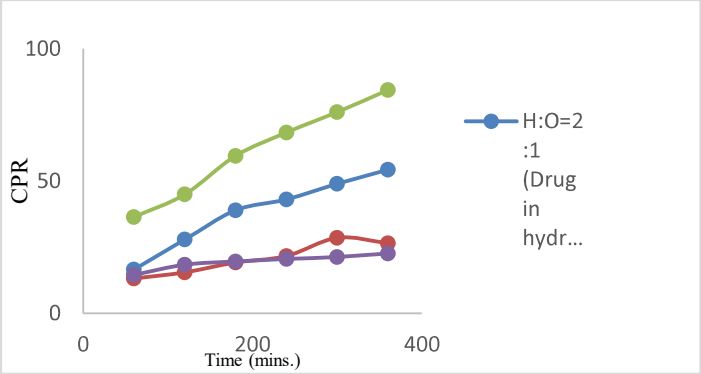

Fig 1: Drug Release profile from bigels in phosphate buffer pH 5.8 at temperature 32^0C

Table 1: Evaluation parameters of bigels

Formulations	Colour	Odour	Appearance	pH	Extrudibility (cm/sec)	% Spreadability (using 10-100gm)
F_1 (1:1) [Drug in hydrogel]	Whitish yellow	odourless	Smooth non-oily	5.5	0.6-0.9	27-72
F_2 (1:1) [Drug in oleogel]	Whitish yellow	odourless	Smooth non-oily	5.5	0.7-0..9	21-77
F_3 (2:1) [Drug in hydrogel]	Whitish yellow	odourless	Smooth non-oily	5.5	0.6-0.9	28-69
F_4 (2:1) [Drug in oleogel]	Whitish yellow	odourless	Smooth non-oily	5.5	0.6-0.9	22-70

Current Trends in **Pharmaceutical Research** 2018, 5(2):28-29
ISSN 2310-4820

www.dibru.ac.in/ctpr

ENHANCED CARDIOPROTECTIVE ACTIVITY OF PHYTOSOMAL NANOCARRIERS OF GREEN TEA POLYPHENOL: FORMULATION AND *IN VITRO-VIVO* EVALUATION

Bhupen Kalita, Pranjal Ray
Girijananda Chowdhury Institute of Pharmaceutical Science, Guwahati-781017, Assam.

Abstract:

Background: Green tea leaves contain epigallocatechin 3-O-gallate (EGCG), a polyphenolic compound as the key component (Huo et al 2008). In spite of many beneficial effects of green tea polyphenols, these suffer from erratic oral bioavailability (Higdon & Frei 2003). Limited GI stability and poor lipophiliciity to cross cell membrane are considered as the main reasons of inadequate bioavailability (Chen et al 2001; Lu et al 2003). Phyto-Phospholipid complexes (Phytosomes) are tailored novel drug carrier designed to improve bioavailability and stability of the standardized herbal extract (Bombardelli et al 1989).
Objectives: The objectives of this study include formulation of EGCG-phospholipid complex (EPC) in attempt to improve cardioprotective efficiency.
Methods: Anti-solvent precipitation method was applied to formulate EGCG-Phospholipid complex (EPC) using varied ratios of green tea extract and phosphatidylcholine (PC). EPCs were characterized by solubility, partition coefficient, particle size, drug content, DSC, FTIR, SEM and *in vitro* dissolution study. Optimized batch of EPC was examined for cardioprotective activity in isoproterenol (ISO)-induced (85 mg/kg, sc) myocardial necrosis in rats.
Results & Discussion: The average particle size of the EPCs was in the range of 200 nm. Drug content of all formulations was found between 85-90%. FT-IR and DSC data confirmed formation of phytosomal complex. SEM images depicted that prepared EPC particles were of spherical in shape with smooth surface texture. Cumulative drug release of the optimized EPC was 98.41% at 3 hrs and followed first order kinetic. In the blood serum

*E-mail: bhupenkalita7@gmail.com; Contact no: +91-8486002671

analysis, increases in the serum marker enzymes- aspartate aminotransferase (AST), alanine transaminase (ALT), lactate dehydrogenase (LDH) and creatine phosphokinase (CPK) were observed in ISO-treated rats compared with normal rats. EPC treatment (100 mg/kg) demonstrated a significant decrease in enzyme elevations.

Conclusions: The findings of the present work demonstrate that nano-sized phytosomes complexes of EGCG result in enhanced cardioprotective response than free form of standardized EGCG.

References:

1. Huo C, Wan SB, Lam WH, Li L, Wang Z, Landis-Piwowar KR, Chen D, Dou QP, Chan TH (2008). The challenge of developing green tea polyphenols as therapeutic agents. Inflammopharmacology, 16(5):248-252.
2. Higdon JV, Frei B (2003). Tea catechins and polyphenols: health effects, metabolism, and antioxidant functions. Crit Rev Food Sci Nutr, 43:89-143.
3. Chen Z, Zhu QY, Tsang D, Huang Y (2001). Degradation of green tea catechins in tea drinks. J Agric Food Chem, 49:477-482.
4. Lu H, Meng X, Yang CS (2003). Enzymology of methylation of tea catechins and inhibition of catechol-O-methyltransferase by (-)-epigallocatechin gallate. Drug Metab Dispos, 31:572-579.
5. Bombardelli E Curri SB, Della RL, Della NP, Tubaro A, Garibodli P (1989). Complexes between phospholipid and Vegetal Derivatives of Biological Interest. Fitoterapia, 60: 1-9.

Current Trends in **Pharmaceutical Research** 2018, 5(2):30-31
ISSN 2310-4820

www.dibru.ac.in/ctpr

ASSESSMENT OF THE EFFECT OF SURFACE MODIFICATION ON THE *IN VIVO* BRAIN TARGETING EFFICIENCY OF ZIDOVUDINE LOADED NANOSTRUCTURED LIPID CARRIERS (NLCS) IN RATS.

Tapash Chakraborty*[1,2], Malay K Das[2], Sanjoy Das[2]
[1]Girijananda Chowdhury Institute of Pharmaceutical Science, Guwahati, 781017
[2]Department of Pharmaceutical Sciences, Dibrugarh University, Dibrugarh, 786004

Abstract:

Background: The blood-brain barrier (BBB) resists the entry of most of the anti-HIV drugs like Zidovudine to the brain. NLCs have been proven to deliver different drugs into the brain[1]. To protect the drug carriers from the reticuloendothelial system and to make them long blood-circulating, developers coat them with different hydrophilic materials like PEG and HSA[2].
Objective: The aim of the present study was to develop brain targeted Zidovudine-loaded NLCs and evaluate the effect of PEG4000 & human serum albumin (HSA) coating on the brain targeting efficiency of the formulation on rats through intravenous route.
Methods: Zidovudine-loaded NLC formulations were developed with oleic acid and Docosanol by modified emulsion technique using Tween 80 as a surfactant. Drug & lipids were mixed with Ethanol by heating at 55˚C. Tween 80 was mixed with water by heating to 55˚C in a separate beaker. The organic phase was slowly added to the aqueous phase under stirring followed by ultrasonication. Ethanol was removed from formulation by continuous stirring. NLCs were then coated with 1%w/v PEG4000 & HSA. The particle size, zeta potential, drug entrapment efficiency, drug loading, and *in vitro* drug release properties of the NLC formulations in PBS (pH 7.4) & in artificial cerebrospinal fluid were determined. The brain drug delivering capability the formulations were studied by injecting them through the tail vein of rats followed by determining the drug concentration in plasma and in the brain with HPLC.
Results & Discussion: The uncoated NLCs had a mean diameter of 54.5±1.3nm and a zeta potential of -21.6±0.2 mV. PEG-coated NLCs had a mean diameter of 57.5±2.2nm and zeta potential of -26±0.7mV. HSA-coated NLCs had a mean diameter of 59.6±1.7nm and a zeta potential of -38.5±0.9

*E-mail: tapash.mpharm@gmail.com; Contact no: 7002926378

mV. The size and spherical shape of the formulations were visualized by scanning electron microscopy and transmission electron microscopy. The *in vivo* study revealed that the coated NLCs achieved a higher plasma C_{max} in rats as compared to the aqueous Zidovudine solution. This may be due to the long blood circulation time of the coated NLCs. It also showed that the drug solution couldn't deliver the drug into the rat brain, but the uncoated NLCs successfully delivered and maintained the drug concentration above its MIC (150 nm/ml) in the brain for more than 24 h. Though the coated NLCs also delivered the drug to the rat brain, their attained concentration was lesser than the uncoated formulation. On coating, the NLCs became more electronegative. Due to this, the electronegative BBB might have repulsed the entry of the coated NLCs to the rat brain leading to their poor brain targeting efficiency.

Conclusion: From the study results it can be concluded that the PEG4000/HSA coating helped the NLCs to attain a long blood circulation time. But, as it became more electronegative upon coating, its brain-targeting efficacy got reduced.

References:

1. Chen Y, Pan L, Jiang M, Li D, Jin L. Nanostructured lipid carriers enhance the bioavailability and brain cancer inhibitory efficacy of curcumin both *in vitro* and *in vivo*. Drug Deliv. 2016; 23(4):1383-1392.
2. Allen TM, Hansen C, Martin F, Redemann C, Yau-Young A. Liposomes containing synthetic lipid derivatives of poly(ethylene glycol) show prolonged circulation half-lives *in vivo*. Biochim Biophys Acta. 1991; 1066(1):29-36.

Current Trends in **Pharmaceutical Research** 2018, 5(2):32-33
ISSN 2310-4820

www.dibru.ac.in/ctpr

EFFICACY OF POLYSORBATE COATED POLYCAPROLACTONE NANOPARTICLES TO IMPROVE THE BRAIN TARGETED DELIVERY OF NEVIRAPINE

Sunita Lahkar*, Malay Kumar Das
Department of Pharmaceutical Sciences, Dibrugarh University, Dibrugarh 786004, Assam.

Abstract:

Background: The Blood-brain barrier (BBB) restricts the entry of most of the drugs (conventional therapy) related to the treatment of neurological disorders such as HIV-encephalopathy, causing the death of billions of people worldwide every year. Nevirapine, an antiretroviral drug when incorporated in the conventional therapy known as highly active antiretroviral therapy (HAART) suffers from poor bioavailability in the brain, patient incompliance, and liver toxicity etc (Saksena et al, 2005). Nanoparticles, size <100 nm, are considered as one of the best strategies based on passive diffusion for brain-targeted delivery of drugs.

Objective: To improve the brain targeted sustained release delivery of Nevirapine incorporated in Polysorbate 80 coated Polycaprolactone nanoparticles.

Methods: The nanoparticles were prepared by emulsion solvent evaporation technique. The biodistribution of the nanoparticles in the brain and other organs such as liver, kidney, spleen, and blood were evaluated in healthy male Wister rats (150 – 200) gm following intravenous administration. The drug level in different organs were estimated using High-performance liquid chromatography (HPLC) (Ambruosi et al,2006). The brain targeting efficiency was determined using confocal laser scanning microscopy (CLSM) (Reimold et al, 2008).

Results and Discussion: The biodistribution study showed that the coated nanoparticles could release the drug and maintained its concentration in the brain for 24 h with the maximum drug concentration obtained at 4 h. While the unmodified nanoparticles could maintain the concentration of drug in the brain for 6 h. For free drug suspension, no drug concentration was detected in the brain. The coated nanoparticles were uniformly distributed in the brain

*E-mail: sunitalahkar@gmail.com

tissues over a period of 24 h with an intense fluorescence observed by CLSM at 4 h.

Conclusion: These results showed that the Polysorbate 80 coated Polycaprolactone nanoparticles could efficiently deliver Nevirapine to the brain maintaining its concentration for 24 h. Thus, Polysorbate 80 coated Polycaprolactone nanoparticles have a good scope in the field of medical interventions for the treatment of most of the neurological disorders.

Keywords: BBB, Nevirapine, Polycaprolactone, Polysorbate 80, Emulsion solvent evaporation technique, CLSM.

References

1. Ambruosi A, Khalansky AS, Yamamoto H, Gelperina SE, Begley DJ, Kreuter J (2006). Biodistribution of polysorbate 80-coated doxorubicin-loaded [14C] - poly (butyl cyanoacrylate) nanoparticles after intravenous administration to glioblastoma-bearing rats. J Drug Target, 14: 97–105.
2. Reimold I, Domke D, Bender J, Seyfried CA, Radunz HE, Fricker G(2008). Delivery of nanoparticles to the brain detected by fluorescence microscopy. Eur J Pharm Biopharm, 70:627-632.
3. Saksena NK, Smit TK (2005).HAART & the molecular biology of AIDS dementia complex.Indian J Med Res, 121(4):256-269.

Current Trends in **Pharmaceutical Research** 2018, 5(2):34-35
ISSN 2310-4820

www.dibru.ac.in/ctpr

METALLIC NANOMATERIALS AS ALTERNATIVE TO CONVENTIONAL ANTIBIOTICS

Dev Jyoti Kalita*[1], Bibhuti B. Kakoti[1], Rima Moni Doley[2], Sanjeeb Kakati[2]

[1]Department of Pharmacceutical Sciences, Dibrugarh University, Dibrugarh-786004

[2]Department of Medicine, Assam Medical College and Hospital, Dibrugarh-786002

Abstract:

Background: The rampat use and abuse of antibiotics has led to the emergence of multidrug-resistant bacterias and super-bacteria as they carry a super-resistance gene called NDM-1. Also most bacteria form a biofilm, within which bacterias can produce superantigens to evade the immune system. Metallic nanoparticles (MNPs) are increasingly used to target bacteria as an alternative to antibiotics and are advantageous in treating bacterial infections (Wang et *al* 2017). Most of the antibiotic resistance mechanisms do not apply for MNPs because the mode of action is direct contact with the bacterial cell wall, without the need to penetrate the cell, thus MNPs would be less prone to develop resistance in bacteria than antibiotics.

Objectives: The development of new drugs and alternative ways to fight bacterial resistance is the need of the hour to combat infectious diseases effectively. MNPs are emerging as potential future drugs to treat bacterial infections. It is necessary to review and study various MNPs for their antibacterial activity and their different modes of action for further development new antimicrobial agents for clinical use.

Methods: A thorough literature survey was carried out from various published research and review articles to compile various mechanisms of actions of MNPs and effectiveness of some of most promising MNPs against different pathogenic and resistant bacterial species.

Result and Discussions: The multifaceted bactericidal actions of MNPs include ROS generation, disorganization of bacterial membrane,

*E-mail: devkalita@gmail.com; Contact. no: +91-9733020389

intercalation between DNA bases, adsorption of nanomaterial to bacterial cell (electrostatic interaction), alteration in bacterial membrane permeability, penetration of the cell envelope and ribosome destabilization, disruption of bacterial biofilms and also immunomodulatory effects of metal nanomaterials (Hemeg 2017).

Several inorganic metals and their oxides in the form of nanoparticles including Ag, TiO_2, CuO, Fe_3O_4, ZnO, Au have been studied and reported for their potential antimicrobial activities against different pathogenic Gram positive, Gram negative and resistant bacterial species such as MRSA. AgNPs has broad-spectrum antimicrobial activity against bacteria, fungi, and viruses, which is termed "oligodynamic activity". Studies have also shown that many metallic NPs prevents biofilm formation due to its smaller size and higher surface area-to-mass ratio and the particle shape of MNPs also has a effect on biofilm destruction (e.g. MNPs with a rod like shape are more effective than spherical shape MNPs).

Conclusion: In this review, we discussed the antibacterial mechanisms of MNPs and various MNPs which are reported to active against different species of pathogenic and resistant bacterial species. In an era of increasing MDR, MNPs are a viable alternative to antibiotics and appear to have high potential to solve the problem of the emergence of bacterial MDR. The current review may contribute to the development of efficient antibacterial MNPs.

References:

1. Wang L, Chen Hu and Shao L (2017).The antimicrobial activity of nanoparticles: present situation and prospects for the future. Int J Nanomed, 12: 1227–1249.
2. Hemeg H A (2017). Nanomaterials for alternative antibacterial therapy. Int J Nanomed, 12: 8211–8225.

Current Trends in **Pharmaceutical Research** 2018, 5(2):36
ISSN 2310-4820

www.dibru.ac.in/ctpr

A REVIEW ON TREATMENT OF ALZHEIMER'S DISEASE WITH THERAPEUTIC NANOPARTICLES

Quri Kiron Hazarika*, Deepsikha Bharali
Department of Pharmaceutical Sciences, Dibrugarh University, Dibrugarh, Assam-786004

Abstract:

Background: For successful therapy of Alzheimer's Disease (AD), safe and effective delivery of therapeutic nanoparticles to the brain is important.
Objective: In this review, Alzheimer's disease and its treatment with therapeutic nanoparticles are highlighted.
Method:_ To this prospect a broad literature review was carried to study the different therapeutic nanoparticles, which are used to treat the Alzheimer's disease.
Results and Discussions: AD is a progressive neurodegenerative disorder characterized by memory loss, cognition and behavioral impairment. These situations can be improved by treatment with therapeutic nanoparticles such as Lf-TMC-NPs (Lactoferin -conjugated N-trimethylated chitosan) and PLGA (zinc loaded polyactide co-glycolide) based nanoparticles. Lf-TMC-Nps has good sustained release effect, adhesion and targeting ability to improve the Alzheimer's condition (1) and the PLGA based Nps improved the Alzheimer's disease by reducing the plaques formation (2).
Conclusion: To treat AD is very difficult and currently there is no cure but these therapeutic nanoparticles has some positive effect to cure or to improve the symptoms of this disease and that's why this nanotargeted treatment has a great future prospect.

Key Words: Alzheimer's Disease, Therapeutic Nanoparticles, Lf-TMC-NP's, PLGA.

References

1. Antonietta Vilella et al. Reduced plaque size and inflammation in the APP23 mouse model for Alzheimer's disease after chronic application of polymeric nanoparticles for CNS targeted zinc delivery. Journal of Trace Elements in Medicine and Biology, 49, (2018), 210–221.
2. Govindarajan Karthivashan et al. Therapeutic strategies and nano-drug delivery applications in management of ageing Alzheimer's disease. Drug Delivery, 25(1), (2018), 307–320.

*E-mail: qurikiron25@gmail.com , Contact no- 08486446807

Current Trends in **Pharmaceutical Research** 2018, 5(2):37
ISSN 2310-4820

www.dibru.ac.in/ctpr

BIOINTERACTION OF NANO MATERIALS; CHALLENGES AND SOLUTIONS

Afsana Khan*, Abhik Das
Department of Pharmaceutical Sciences, Dibrugarh University, Dibrugarh, Assam

Abstract:

The nanotechnology has gained a great deal of public interest because of the needs and applications of nanomaterials in many areas of human and endeavors including industry, agriculture, business, medicine and public health. Environmental exposure to nanomaterials is inevitable as nano materials becomes part of our daily life and thus nano toxicity research is gaining attention [1]. Bio-interaction of nano materials addresses the issues related to toxicity and safety of nano material and nano systems. It covers the interaction in biological systems and presents various tools and methods used to evaluate the nano toxicity and nano safety issues [2]. Nano safety is one of the prime importances in creating a sustainable nanotechnology environment. Moreover, biocompatibility of nanoparticles depends on number of factors that include size, shape, surface chemistry, surface charges, surface reactivity, protein corona, dose, route of exposure, biological host etc. It is necessary to overcome the challenges of nano toxicity in different fields. This paper presents a summary of recent research efforts on fate behavior and toxicity of different classes of nano materials on different fields mentioned above.

Key Words: *Nanomaterials, Bio-interaction, Nanotoxity, Biocompatibility, Nanosafety.*

References:

1. Roy P. C., "Toxicity and Environmental Risks of Nanomaterials: Challenges and Future needs", J Environ Sci Health C Environ Carcinog Ecotoxicol Rev, 2009, 27(1): 1-35.
2. Sutariya V. B., Pathak Y., "Biointeraction of Nanomaterials",1st Edition,CRC Press, New York, 2014.

*E-mail: afsanak091@gmail.com

Current Trends in **Pharmaceutical Research** 2018, 5(2):38-39
ISSN 2310-4820

www.dibru.ac.in/ctpr

NANOPESTICIDES FOR PREVENTING MEDICINAL PLANTS FROM DESTRUCTIVE PEST- A REVIEW

Lalruatfeli*[1], B.B.Kakoti[1]
Department of Pharmaceutical Sciences, School of Science and Engineering, Dibrugarh University, Dibrugarh-786004, Assam

Abstract:

Background: Medicinal plants, nowadays has been exceedingly employed globally for its treatment of diseases. Many important medicinal plants are on the verge of extinction from various threats. Pests are such organisms responsible for the cause. Moreover, the quantity of secondary metabolites production in plants is being affected by various pests (Pimentel 2009). Nanotechnology is essential for preserving biodiversity in order to improve the synthetic chemical pesticides which can be utilized as nanopesticides (Chhipa 2017). Medicinal plants are commonly used for pharmaceutical preparations, supplements, and mostly for self- medication or prescribed by the folk healers or consumed as edible purposes. There are ample scopes and possibilities of using nanopesticides replacing the conventional pesticides which have better protection, performance and are also environmental friendly(Khater 2012).

Objective: To describe the scope of nanopesticides over conventional pesticides and to study the ways in which adverse effect of the conventional pesticides can be reduced for avoiding wastage of the active ingredient.

Methods: The review is carried out by exhaustive literature survey. Medicinal plants infected by pest were selected and some pesticides with its effect on human, insects and animals. The technique of environmental responsive delivery systems was selected.

Results & Discussion: It was found that targeted delivery and controlled release of nanomaterial can improve pesticide utilization and reduce residue and pollution. Pesticide nanocapsule formulations have slow release and protection performance and due to their small size, improvable pesticide droplet ductility, wettability, and target adsorption when spraying in fields provide efficient and environmental friendly results and outcomes (Chhipa 2017).

*E-mail: ngfeliralte67@gmail.com, Contact no. +91-7085844868

Conclusion: In the future, controlling pests by environmentally responsive delivery systems will ameliorate the yield and quality of medicinal plants by analysing the pest profile and level prior to using the nanopesticides. Hence, the use of nanopesticides over conventional pesticides has more chance of beneficial effect on the medicinal plants and huge loss while spraying can be minimised and prevented.

Key Words: Nanotechnology, nanopesticides, medicinal plants, delivery system.

References:

1. Pimentel D (2009). Pesticides and pest controls. In Integrated Pest Management: Innovation Development process, Peshin R, Dhawan AK (eds.), Volume 1, pp. 83-87. DOI 10.1007/978-1-4020-8992-3_3
2. Khater HF (2012). Prospects of botanical biopesticides in insect pest management. Pharmacologia, 3(12):641-656. DOI: 10.5567/pharmacologia.2012.641.656
3. Chhipa H. (2017). Nanopesticide: Current Status and Future Possibilities. Agricultural Research & Technology, 5(1): 555651. DOI: 10.19080/ARTOAJ.2017.05.555651

Current Trends in **Pharmaceutical Research** 2018, 5(2):40-41
ISSN 2310-4820

www.dibru.ac.in/ctpr

EVALUATION OF ANXIOLYTIC ACTIVITY OF *ZANTHOXYLUM ALATUM* AND *DYSPHANIA AMBROSIODES* ON MICE

Rajashri Bezbaruah[1], Chandana C. Barua[2], Rupshikha Malakar[3]
[1]Pratiksha Institute of Pharmaceutical Sciences, Panikhaiti, Guwahati, Assam
[2] Department of Pharmacology and Toxicology, College of veterinary science, Guwahati, Assam
[3]Royal college of pharmacy and health sciences, Berhampur, Orissa.

Abstract:

Background: Anxiety is a psychological and physiological state of unpleasant feeling that is typically associated with uneasiness, apprehension, fear, or worry (Mesfin *et. al* 2014).Leaves of *Dysphania ambrosiodes* have been used as an alternative to tea in Mexico.Traditionally this plant is used for expelling parasites or worms, digestive disorders, malaria, hysteria and other nervous diseases and asthma. (Yadav *et. al.*2007)**.** The fruits and seeds of *Zanthoxylum alatum* is employed as an aromatic tonic in fever, carminative, stomachic, anthelmintic. The volatile oil is employed as an antidiarrheal, antiseptic etc. (Prakash *et. al.* 2012)

Objective: The present study investigates the anxiolytic effects of crude extractsfrom dried leaves of *Zanthoxylum alatum*(ZAHE) and*Dysphania ambrosiodes* (DAHE) on mice using elevated plus maze (EPM), light and dark model, open field model (OFT) and hole board model.

Materials and Methods: Two oral doses (100 and 200 mg/kg) of the crude hydroethanolic extract of *Zanthoxylum alatum*(ZAHE) and*Dysphania ambrosiodes* (DAHE) were evaluated for anxiolytic activity by elevated plus maze (EPM), light and dark model, open field model (OFT) and hole board model. Anxiety was induced by isolating animals socially for 21 days. Diazepam was used as standard anti anxiety drug at a dose of 2 mg/kg, *i.p*.

Results: The test drugs were compared with standard drug and control by one-way analysis of variance (ANOVA) followed by Dunnett's multiple comparison test.All the treatments showed a significant ($P< 0.005$) increase in all parameters number of entries in the open arm and time spent in the open arms (Elevated Plus maze), the time spent in the light compartment by the mice (Light and dark model), Numbers of rearing and number of squares

*E-mail: rajashribezbaruah3@gmail.com, Contact no: +91-7002650627

crossed (Open field method), Number of head dips in the holes (Hole board method) when compared with the negative control.

Conclusion: These results indicated that dried leaves of *Zanthoxylum alatum*(ZAHE) and *Dysphania ambrosiodes* (DAHE) might become a promising therapeutic agent for the treatment of antianxiety dysfunction in addition to its already established medicinal properties.

Reference:

1. Mesfin M, Asres K, Shibeshi W (2014).Evaluation of anxiolytic activity of the essential oil of the aerial part of Foeniculum vulgare Miller in mice. BMC Complementary and Altern Med. 14(310):1-7.
2. Yadav N, Nasudeva N,Singh S, Sharma S (2007). Medicinal properties of genus *Chenopodium* Linn.Nat Prod Rad.6(2):131-134.
3. Prakash B,SinghP, Mishra PK,Dubey NK(2012). Safety assessment of *Zanthoxylum alatum* Roxb. essential oil, its antifungal, antiaflatoxin, antioxidant activity and efficacy as antimicrobial in preservation of *Piper nigrum* L. fruits.Int. J. Food. Microbiol.153(1–2):183-191.

Current Trends in **Pharmaceutical Research** 2018, 5(2):42-43
ISSN 2310-4820

www.dibru.ac.in/ctpr

ACTIVE TARGETING "SMART" NANOVECTORS: PROSPECTS IN THE DEVELOPMENT OF BREAST CANCER CHEMOTHERAPY

Sushmita Sahu [a*], Urvashee Gogoi [a,b] , Aparoop Das [a]
[a]Department of Pharmaceutical Sciences, Dibrugarh University
[b]Himalayan Pharmacy Institute, Majhitar, Sikkim

Abstract:

Background: Breast cancer is the second most common cancer worldwide after lung cancer, the fifth most common cause of cancer death, and the leading cause of cancer death in women. The statistics are grim worldwide and the global burden of breast cancer is expected to cross 2.5 million by the year 2030 [1]. Despite exciting progress in the understanding of breast cancer development and progression, and in the development of novel therapeutic strategies, women continually suffer from side effects of the drugs and often acquire resistance leading to relapse and metastasis.
Objective: The current review summarizes recent developments in active targeting nanomolecular agents with various targeting moieties and describes the current status of and challenges in the field of nanocarrier-aided drug delivery and drug targeting systems.
Methods: Relevant English electronic databases and scientifically published original articles and reviews were systematically searched for the purpose of this review.
Results and Discussion: Conjugation of cell-specific ligands (including antibodies) to the surface of nanoscale drug carriers can potentially increase delivery of a therapeutic agent to a desired anatomic site, while decreasing unwanted delivery to other sites [2]. This targeting strategy is based on the molecular recognition of tumor biomarkers which are over-expressed on cancer cells, via specific vector molecules conjugated to the surface of the drug carrier. These vector molecules dictate the carrier's biodistribution and its biological affinity to the desired site of action [3,4,5].
Conclusion: This strategy commonly known as active targeting may be the answer to the present woes of breast cancer patients.

Key Words: Nanocarriers, breast cancer, targeted-therapy, ligand-targeting.

*E-mail: urvashigogoi777@gmail.com, Phone no.: +91-8638168581

References:

1. Jemal, A., Bray, F., Center, M. M., Ferlay, J., Ward, E., & Forman, D. (2011). Global cancer statistics. CA: A Cancer Journal for Clinicians, *61*(2), 69-90.
2. Bazak, R., Houri, M., El Achy, S., Kamel, S., & Refaat, T. (2015). Cancer active targeting by nanoparticles: a comprehensive review of literature. Journal of Cancer Research and Clinical Oncology, 141(5), 769-784.
3. Karra, N., & Benita, S. (2012). The ligand nanoparticle conjugation approach for targeted cancer therapy. Current Drug Metabolism, 13(1), 22-41.
4. Muhamad, N., Plengsuriyakarn, T., & Na-Bangchang, K. (2018). Application of active targeting nanoparticle delivery system for chemotherapeutic drugs and traditional/herbal medicines in cancer therapy: a systematic review. International Journal of Nanomedicine, 13, 3921-3935.
5. Marina S F, Marjorie C R, Monica C O. Active Targeting of Breast Cancer Cells Using Nanocarriers. Modern Application in Pharmacy & Pharmacology, 1(2). MAPP.000507. 2017. DOI: 10.31031/MAPP.2017.01.000507