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Pharmacokinetics and Pharmacodynamics Characteristic Study of Ophthalmic Drugs: A Milligram Level Estimation

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Abstract: *Ophthalmic drug delivery is one of the most interesting and challenging endeavors facing the pharmaceutical scientists. The anatomy, physiology and biochemistry of the eye render this organ exquisitely impervious to foreign substances. The challenge to the formulator is to circumvent the protective barriers of the eye without causing permanent tissue damage. The development of newer, more sensitive diagnostic techniques and therapeutic agents renders urgency to the development of more successful ocular delivery systems. Potent immunosuppressant therapy in transplant patients and the developing epidemic of AIDS have generated an entirely new population of patients suffering virulent uveitis and retinopathies.*

Background*: Ophthalmic drug delivery is one of the most interesting and challenging endeavors facing the pharmaceutical scientists. The anatomy, physiology and biochemistry of the eye render this organ exquisitely impervious to foreign substances. The challenge to the formulator is to circumvent the protective barriers of the eye without causing permanent tissue damage. The development of newer, more sensitive diagnostic techniques and therapeutic agents renders urgency to the development of more successful ocular delivery systems. Potent immunosuppressant therapy in transplant patients and the developing epidemic of AIDS have generated an entirely new population of patients suffering virulent uveitis and retinopathies.*

Materials and Methods*: Aliquots containing 1-5 mg of the sample were taken in 100 ml stoppered conical flask followed by the addition of 5ml AHC (0.1 M) reagent, prepared in 0.5N HNO_3. The reaction mixture was shaken well and allowed to react for required reaction time at room temperature (25-30ºC). The unconsumed Ce(IV) was titrated against 0.025M FAS solution using two drops of ferroin indicator (0.001M). A blank experiment was also performed under identical conditions using all the reagents except the sample. The amount of AHC consumed for the sample was calculated with the difference in the titre values of ferrous ammonium sulphate solution for blank and actual experiments.*

Results*: The ophthalmic drugs are an important group of therapeutic compounds used for a variety of clinical purposes. Despite the numerous achievements in the field of ophthalmic dosage forms, the vast majority of the active ingredients are still in the form of eye drops for use in eye disorders. Some of the more complex forms have appeared in the pharmaceutical market, but scientists are still looking for the right ophthalmic system that has the desired properties such as controlled release, minimization of systemic effects, ease of use and time storage on the application site. Multicompartment systems appear to be promising forms of medicine which can also be combined with other forms.*

Conclusion: *Despite the numerous achievements in the field of ophthalmic dosage forms, the vast majority of the active ingredients are still in the form of eye drops for use in eye disorders. Some of the more complex forms have appeared in the pharmaceutical market, but scientists are still looking for the right ophthalmic system that has the desired properties such as controlled release, minimization of systemic effects, ease of use and time storage on the application site. Multicompartment systems appear to be promising forms of medicine which can also be combined with other forms.*

Key Word*: Milligram Level Determination, Ophthalmic Drugs*

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I. Introduction

Ophthalmic drug delivery is one of the most interesting and challenging endeavors facing the pharmaceutical scientists. The anatomy, physiology and biochemistry of the eye render this organ exquisitely impervious to foreign substances. The challenge to the formulator is to circumvent the protective barriers of the eye without causing permanent tissue damage. The development of newer, more sensitive diagnostic techniques and therapeutic agents renders urgency to the development of more successful ocular delivery systems. Potent immunosuppressant therapy in transplant patients and the developing epidemic of AIDS have generated an

entirely new population of patients suffering virulent uveitis and retinopathies. The primitive Ophthalmic solution. suspension and ointment dosage forms are clearly no longer sufficient to combat these diseases.

Different types of Ophthalmic have dissimilar actions in the different disease. An antimusearinic agent such as Cyclopentolate hydrochloride, Atropine sulphate and tropicamide are used as eye drops to produce cycloplegia and mydriasis. Ophthalmic (hugs of aminoglycoside group such as Gentamicin sulphate, Tobramycin sulphate and Neomycin sulphate are active against Gram-negative bacteria. Fluoroquinolone antibacterial agent such as Ciprofloxacin and Norfloxacin are active against Gram- Positive bacteria.

In the present paper, a simple method for the quantitative determination of following Ophthalmic drugs such as Cyclopentolate hydrochloride, Atropine sulphate, Gentamicin sulphate, Ciprofloxacin hydrochloride, Niometacin, Tobramycin sulphate, etc. Chemically Cyclopentolate hydrochloride is 2-(dimethylamino) ethyl (I-hydroxycyclopentyl) (phenyl) acetate hydrochloride. Cyclopentolate hydrochloride is a white crystalline powder. It is soluble in water and practically insoluble in ether. Cyclopentolate is a mydriatic and cycloplegic agent commonly used during pediatric eye examinations. Cyclopentolate is also administered as an Atropine substitute to reverse muscarinic and CNS effects of indirect cholinomimetic (anti-AChase) administration. When used in eye drops in pediatric eye examinations, Cyclopentolate 0.5% and 1.0% is used to stop the eye focusing at near distance, enabling the optometrist or ophthalmologist to obtain a more accurate reading of the focusing power of the eyes.

The drops take around 30 minutes to work and around 24 hours to wear off (with patients advised not to drive a vehicle or operate machinery for the first 12 hours). The pupils become wider when Cyclopentolate is administered, making the eyes more sensitive to light. Close objects (and possibly distant objects) will also appear blurred. Side effects to Cyclopentolate are rare, but can include effects such as disorientation, incoherent speech or visual disturbances during the 24-hour period that the drug has an effect.

Literature survey reveals that very few analytical methods such as non-aqueous titration] and HPLC have been reported for the determination of Cyclopentoiate hydrochloride. Kannarao, K.V., and co-workers reported estimation of Cyclopentolate hydrochloride from Ophthalmic solutions. Andermann, G., and co-workers' reported determination of Cyclopentolate by capillary column gas-liquid chromatography. Mordi, j., and co-workers reported effects of 1% Cyclopentolate on pupil diameter and accommodation.

Atropine Sulphate slightly soluble in chloroform and practically insoluble in solvent ether. It is a competitive antagonist for the muscarinic acetylcholine receptor. Tropical Atropine is used as a cycloplegic, to temporarily paralyze the accommodation reflex, and as a mydriatic, to dilate the pupils. Atropine induces mydriasis by blocking contraction of the circular pupillary sphincter muscle, which is normally stimulated by acetylcholine release, thereby allowing the radial pupillary dilator muscle to contract and dilate the pupil. Atropine induces cycloplegia by paralyzing the ciliary muscles, whose action inhibits accommodation to allow accurate refraction in children, helps to relieve pain associated with iridocyclitis, and treats ciliary block (malignant) glaucoma.

Because of its great medicinal utilization, a large number of procedures have been p developed for its determination. Kirchhoff, C., and co-workers reported analysis of Atropine, its degradation products and related substances of natural origin by means of reversed-phase high-performance liquid chromatography. Adams, M., and co-workers p reported HPLC-MS trace analysis of Atropine in Lyceum barbarum berries. Carstensen, S; and co-workers reported quantitative analysis of dobutarnine-Atropine stress echocardiography by fractional area change. Bhat, K. M; and co-workers reported development of a new spectrophotometric method for the analysis of Atropine sulphate. Ahmet. G; and co-workers' reported simple high-performance liquid chromatographic method for determination of Atropine and obidoxime in a parenteral injection device. Chua, W; and co-workers reported analysis of safety data for Atropine in the treading of myopia (ATOM) Study. Charkaoui, S; and co-workers reported validated capillary electrophoresis method for the determination of Atropine and scopolamine derivatives in pharmaceutical formulations. Takahashi, M., and co-workers reported Determination of Atropine in pharmaceutical preparations by liquid chromatography with fluorescence detection. Elsayed, M.A., and co-workers]5 reported spectrophotometric determination of Atropine, pilocarpine md strychnine with chloranilic acid. Mostafa, G.A.E., and co- workers reported PVC Membrane Sensor for Potentiometric Determination of Atropine in Some Pharmaceutical Formulations.

Gentamicin sulphate is a complex mixture of the sulphates of Gentamicin Ci, Gentamicin Cia and Gentamicin C2. Gentamicin sulphate is in the form of white to buff powder. It is freely soluble in water and practically insoluble in alcohol, acetone, chloroform and ether. Gentamicin is an aminoglycoside antibiotic, used to ueat many types of bacterial infections, particularly those caused by Gram-negative bacteria. However, Gentamicin is not used for Neisseria gonorrhoeae, Neisseria meningitidis or Legionella pneumophila bacterial infections (because of the risk of the patient going into shock from lipid A endotoxin found in certain gram-negative organisms). It is synthesized by Micromonospora, a genus of Gram-positive bacteria widely present in the environment Nater and soil). To highlight their specific biological origins, Gentamicin and other related antibiotics produced by this genus (verdamicin, mutamicin, sisomicin, netilmicin, rerymicin) have generally

their spellings ending in -mycin md not in -mycin. Cientaniicin i.e., bactericidal antibiotic that work by binding thc 30S subunic of the bacterial ribosome. attempting protein synthesis. It is not absorbed by mouth and is usually given intramuscularly or intravenously in severe systemic Gram-negative infections, often in combination with another agent such as betajactam. The main adverse effects are ototoxicity and nehtoxicity, monitoring of plasma concentration, is important to avoid toxic concentrations. Gentamicin is one of the few heat stable antibiotics that remain active even after autoclaving, Which makes it particularity useful in the preparation of certain Microbiological growth media.

Because of its medicinal importance several methods have been developed for its determination and assay. Seral, C., and co-workers reported Quantitative Analysis of Gentamicin, Azithromycin, Telithromycin, Ciprofloxacin, Moxifloxacin, and Oritavancin activities against intracellular Staphylococcus aureus in mouse J774 Macrophages. Stead, DA., and co-workers reported sensitive fluorometric determination of Gentamicin sulphate in biological matrices using solid-phase extraction, pm-column derivatization with 9-fluorenyhnethyl chloroformate and reversed-phase high-performance liquid chromatography. Kaale, E., and co-workers reported capillary electrophoresis analysis p of Gentamicin SdphatC with UV detection after pre-capillary derivatization with 1,2-

phthalic dicarboxaidehyde and mercaptoacetic acid. Chow, J. W., and co-workers reported in vitro susceptibility and molecular analysis of Gentamicin-resistant enterococci. Wang, H.Y., and co-workers reported determination of Gentamicin by synchronous derivative by fluorimetry. Kavimani, S., and co-workers reported interaction between Gentamicin and benidipine hydrochloride. Zhang, Z.J., and co- workers reported flow injection chemiluminescence method for the determination of Gentamicin using cobalt (III) as an oxidant. Chemically Ciprodoxacin hydrochloride is 1-cyclopropyl- 6-fluoro- 4-oxo- 7- piperazin- l-yl-quinoline-bicarboxylic acid hydrochloride.

II. Material and Methods

Aliquots containing 1-5 mg of the sample were taken in 100 mL stoppered conical flask and 5 mL of the $3x10^{-2}$ N PFC reagent, prepared in glacial acetic acid and 10 mL of 5N H_2SO_4 was added to it. The reaction mixture was shaken thoroughly and allowed to excel for required reaction time at room temperature (25-30°C). After the reaction is over 5mL of 10% potassium iodide was added to stand for one minute. The unconsumed PFC was determined iodometrically. A blank experiment was also run under identical conditions using all the reagents except the sample. The amount of PFC consumed for the sample was calculated with the difference in the titer values of sodium thiosulphate solution for blank and actual experiments. The recovery of the sample was calculated with the amount of PFC consumed for the sample. For every sample percentage error, coefficient of variation and standard deviation were calculated.

To evaluate the authenticity of the method recovery experiments were also carried out by standard drug addition method. For such experiments a known amount of the pure drug is taken and varying amounts of the pharmaceutical preparations of that compound are added and the total amount of the sample was found out with titration and calculations.

III. Result and Discussion

As described in the survey of literature, the PFC reagent has not been used for the estimation of adrenocorticosteroid drugs. As described in the survey of literature, the PFC reagent has not been used for the estimation of Ophthalmic drugs. Therefore in the present chapter, a simple method is described for the determination of following Ophthalmic drugs, such as Cyclopentolate hydrochloride, Atropine sulphate, Gentamicin sulphate, Norfloxacin, Ciprofloxacin hydrochloride and Tobramycin sulphate in pure form and in their Ophthalmic Drugs pharmaceutical preparations such as Cyclate(Dps), Cyclogik (Dps), ATP (Dps), Tropine (jjps), Genta Swift (Dps), Intragen (Dps), Normax (Dps), Norflox (Dps), Adiflox (Dps). Zoxan (Dps), Toba (Dps) and Tobramycin (Dps) have been studied.

Approach of the reaction:

For testing the quantitative validity of Cyclopentolate hydrochloride was taken as test sample. Different amount of sample (1-5mg) was allowed to react with varying concentrations of pyridinium fluorochromate (PFC) at boiling water bath temperature for different intervals of reaction time. The unconsumed PFC was back titrated using standardized sodium thiosulphate iodometrically. A blank experiment was also run under identical conditions using all the reagents except the sample. With the difference in the titre values of sodium thiosulphate consumed for blank and actual experiments were used to calculate the amount of the sample present in a particular experiment. The stoichiometry of the reaction was established for each sample and a possible course of reaction was also suggested. On the basis of the reaction conditions developed for Cyclopentolate hydrochloride, the determination of other compounds in the pure form and in their pharmaceutical preparations were done.

Study of variables

In order to develop suitable reaction condition for the milligram determination of above Ophthalmic with PFC reagent the effect of different variables was studied.

Effects of reaction time

Keeping the amount of Cyclopentolate hydrochloride and concentration of PFC reagent as constant, the reaction time was varied from room temperature to boiling water bath temperature. Aliquots containing 5mg of Cyclopentolate hydrochloride were taken in 100 mL stoppered conical flask and 5ml of $3x10^{-2}$N PFC reagent prepared in glacial acetic acid was added to it. Now the reaction mixture was shaken well and allowed to react at boiling water bath temperature for 1-25 minutes. After the reaction was over the concerned PFC was determined by back titrating the reaction mixture against standardized sodium thiosulphate (0.01N) solution using positum iodide and starch as indicator. It was observed that the recovery of the maple becomes constant at reaction time of 10 minutes. The recovery of the sample docs not change after a proper reaction time. Therefore, further estimation was done on the same reaction time. Similar experiments were performed with other maples as well. 11 was observed that all the Ophthahnics require 10 minutes to complete the reaction except Tobramycin sulphate, this takes 15 minutes and Gentamicin sulphate which takes 5 minutes to complete the reaction.

Effect of concentration of sulphuric acid

Keeping the reaction time, amount of Cyclopentolate hydrochloride and concentration of PFC constant the concentration of sulphuric acid was varied from (1-7N) and the results were noted. Results given in the table shows that the best recovery of the samples was obtained at 5N concentration of sulphuric acid. To ascertain the exact amount of 5N sulphuric acid needed for the reaction, some deviations were done in the volume, accurate results were obtained at 10 mL of the acid. Similar results were obtained in case of other Ophthalmics. Thus, for completing the reaction and getting accurate results 10mL of 5N sulphuric acid was recommended for the experiment.

Effect of concentration of PFC

Keeping the reaction time, amount of Cyclopentolate hydrochloride and connumeration of sulphuric acid as constant, the effect of varying concentration of PFC was studied. 5mg of the sample was allowed to react with 5mL of varying concentration (0.01-0.1N) of PFC. The unconsumed PFC was back titrated iodometrically and the recovery of the sample was calculated. It was found that the best results were obtained at 0.03N concentration of PFC. The concentration of reagent less than 0.03N gives higher Percentage error and low recovery. The reason for this is due to incomplete reaction of the reagent with the sample. The higher concentration than 0.03N gives no significant advantage in percentage recovery. Therefore, the higher concentration of the reagent was avoided. Variation in the volume of $3x10^{-2}$N PFC was also studied. It was observed that 5mL of $3x10^{-2}$N PFC gives accurate result. Thus, for completing the reaction, getting accurate results and also avoiding the wattages of the reagent, 5mL of $3x10^{-2}$N PFC was recommended for the experiment. In the similar way the studies of different variables were also done with Cyclopentolate hydrochloride.

Effect of temperature

Keeping all other conditions constant, the reaction temperature was varied from mm temperature to boiling water bath and the recovery of Cyclopentolate hydrochloride was calculated. It was observed that the reaction was completed within 10 minutes at boiling water bath temperature. Although the reaction is completed at boiling water bath temperature, but the experiment was also carried out at lower temperature up to 5°C. In this case also a decrease in recovery of the sample was noted. It shows that the reagent does not react properly at lower temperature. Thus, for the estimation of Cyclopentolate hydrochloride a reaction temperature of boiling water bath was maintained. Such experiments were carried out with dl other samples and the recovery was noted. It was observed that the reaction at boiling water bath temperature was suitable for all other Ophthalmic e.g., Atropine sulphate, Gentamicin sulphate, Norfioxacin, Ciprofloxacin hydrochloride and Tobramycin sulphate.

IV. Conclusion

Despite the numerous achievements in the field of ophthalmic dosage forms, the vast majority of the active ingredients are still in the form of eye drops for use in eye disorders. Some of the more complex forms have appeared in the pharmaceutical market, but scientists are still looking for the right ophthalmic system that has the desired properties such as controlled release, minimization of systemic effects, ease of use and time storage on the application site. Multicompartment systems appear to be promising forms of medicine which can also be combined with other forms.

References

[1]. Draize, J. H.; Woodard, G.; Calvery, H. O., Methods for the study of irritation and toxicity of substances applied topically to the skin and mucous membranes. J. Pharmacol. Exp. Ther. 1944, 82 (3), 377.

[2]. Peyman, G. A.; Sathar, M. L.; May, D. R., Intraocular gentamicin as intraoperative prophylaxis in South India eye camps. Br. J. Ophthalmol. 1977, 61 (4), 260.
[3]. Starr, M. B., Prophylactic antibiotics for ophthalmic surgery. Surv. Ophthalmol. 1983, 27 (6), 353.
[4]. Seifried, H. E., Eye Irritation Testing: Historical Perspectives and Future Directions†. J. Toxicol., Cutaneous Ocul. Toxicol. 1986, 5 (2), 89.
[5]. Grossman, R. E.; Chu, D. F.; Lee, D. A., Regional ocular gentamicin levels after transcorneal and transscleral iontophoresis. Invest. Ophthalmol. Vis. Sci. 1990, 31 (5), 909.
[6]. Gurtler, F.; Kaltsatos, V.; Boisramé, B.; Deleforge, J.; Gex-Fabry, M.; Balant, L. P.; Gurny, R., Ocular availability of gentamicin in small animals after topical administration of a conventional eye drop solution and a novel long acting bioadhesive ophthalmic drug insert. Pharm. Res. 1995, 12 (11), 1791.
[7]. Meisner, D.; Mezei, M., Liposome ocular delivery systems. Adv. Drug Delivery Rev. 1995, 16 (1), 75.
[8]. Cohen, S.; Lobel, E.; Trevgoda, A.; Peled, Y., A novel in situ-forming ophthalmic drug delivery system from alginates undergoing gelation in the eye. J. Controlled Release 1997, 44 (2), 201.
[9]. Anand, V.; Kandarapu, R.; Garg, S., Ion-exchange resins: carrying drug delivery forward. Drug Discovery Today 2001, 6 (17), 905.
[10]. Wilhelmus, K. R., The Draize eye test. Surv. Ophthalmol. 2001, 45 (6), 493.
[11]. Vydrin, A.; Shikhaleev, I.; Makhortov, V.; Shcherenko, N.; Kolchanova, N., Component composition of gentamicin sulfate preparations. Pharm. Chem. J. 2003, 37 (8), 448.
[12]. Elizondo, E.; Córdoba, A.; Sala, S.; Ventosa, N.; Veciana, J., Preparation of biodegradable poly (methyl vinyl ether-co-maleic anhydride) nanostructured microparticles by precipitation with a compressed antisolvent. J. Supercrit. Fluids 2010, 53 (1), 108.
[13]. Popescu, I.; Suflet, D. M.; Pelin, I. M.; Chitanu, G. C., Biomedical applications of maleic anhydride copolymers. Rev. Roum Chim 2011, 56, 173.
[14]. Vandamme, K.; Melkebeek, V.; Cox, E.; Adriaensens, P.; Van Vlierberghe, S.; Dubruel, P.; Vervaet, C.; Remon, J. P., Influence of polymer hydrolysis on adjuvant effect of Gantrez® AN nanoparticles: implications for oral vaccination. Eur. J. Pharm. Biopharm. 2011, 79 (2), 392.
[15]. Pernia Leal, M.; Torti, A.; Riedinger, A.; La Fleur, R.; Petti, D.; Cingolani, R.; Bertacco, R.; Pellegrino, T., Controlled release of doxorubicin loaded within magnetic thermo-responsive nanocarriers under magnetic and thermal actuation in a microfluidic channel. ACS Nano 2012, 6 (12), 10535.
[16]. Fathi, M.; Entezami, A. A., Stable aqueous dispersion of magnetic iron oxide core-shell nanoparticles prepared by biocompatible maleate polymers. Surf. Interface Anal. 2014, 46 (3), 145.
[17]. Rata, D. M.; Popa, M.; Chailan, J. F.; Zamfir, C. L.; Peptu, C. A., Biomaterial properties evaluation of poly (vinyl acetate-alt-maleic anhydride)/chitosan nanocapsules. J. Nanopart. Res. 2014, 16 (8), 1.
[18]. Sur, S.; Fries, A. C.; Kinzler, K. W.; Zhou, S.; Vogelstein, B., Remote loading of preencapsulated drugs into stealth liposomes. Proc. Natl. Acad. Sci. U. S. A. 2014, 111 (6), 2283.
[19]. Aguilar-Rosas, I.; Alcalá-Alcalá, S.; Llera-Rojas, V.; Ganem-Rondero, A., Preparation and characterization of mucoadhesive nanoparticles of poly (methyl vinyl ether-co-maleic anhydride) containing glycyrrhizic acid intended for vaginal administration. Drug Dev. Ind. Pharm. 2015, 41 (10), 1632.
[20]. Jain, A. K.; Sahu, P. K.; Mohan, P.; Jain, S. K., Ion Exchange Resins-Pharmaceutical and Clinical Applications. Asian J. Biomat Res. 2016, 2 (2), 51.
[21]. Yellepeddi, V. K.; Palakurthi, S., Recent Advances in Topical Ocular Drug Delivery. J. Ocul. Pharmacol. Ther. 2016, 32 (2), 67.
[22]. Haim-Zada, M.; Basu, A.; Hagigit, T.; Schlinger, R.; Grishko, M.; Kraminsky, A.; Hanuka, E.; Domb, A. J., Stable polyanhydride synthesized from sebacic acid and ricinoleic acid. J. Controlled Release 2017, 257, 156.
[23]. Joseph, M.; Trinh, H. M.; Cholkar, K.; Pal, D.; Mitra, A. K., Recent perspectives on the delivery of biologics to back of the eye. Expert Opin. Drug Delivery 2017, 14 (5), 631.
[24]. Chen, H.; Jin, Y.; Sun, L.; Li, X.; Nan, K.; Liu, H.; Zheng, Q.; Wang, B., Recent Developments in Ophthalmic Drug Delivery Systems for Therapy of Both Anterior and Posterior Segment Diseases. Colloids Interface Sci. Commun. 2018, 24, 54.
[25]. Dugad, A.; Nalawade, P.; Thakhre, R.; Kakade, S., Ion Exchange Resins: An Novel Approach towards Taste Masking of Bitter Drugs and Sustained Release Formulations with Their Patents. Curr. Pharma Res. 2018, 9 (1), 2656.
[26]. Huang, D.; Chen, Y. S.; Rupenthal, I. D., Overcoming ocular drug delivery barriers through the use of physical forces. Adv. Drug Delivery Rev. 2018, 126, 96.
[27]. Larrañeta, E.; Barturen, L.; Ervine, M.; Donnelly, R. F., Hydrogels based on poly (methyl vinyl ether-co-maleic acid) and Tween 85 for sustained delivery of hydrophobic drugs. Int. J. Pharm. 2018, 538 (1–2), 147.
[28]. Lucio, D.; Martínez-Ohárriz, M. C.; Gu, Z.; He, Y.; Aranaz, P.; Vizmanos, J. L.; Irache, J. M., Cyclodextrin-grafted poly (anhydride) nanoparticles for oral glibenclamide administration. In vivo evaluation using C. elegans. Int. J. Pharm. 2018, 547 (1–2), 97.
[29]. Popilski, H.; Abtew, E.; Schwendeman, S.; Domb, A.; Stepensky, D., Efficacy of paclitaxel/dexamethasone intra-tumoral delivery in treating orthotopic mouse breast cancer. J. Controlled Release 2018, 279, 1.
[30]. Brotons-Canto, A.; Gamazo, C.; Martín-Arbella, N.; Abdulkarim, M.; Gumbleton, M.; Quincoces, G.; Peñuelas, I.; Irache, J. M., Mannosylated Nanoparticles for Oral Immunotherapy in a Murine Model of Peanut Allergy. J. Pharm. Sci. 2019, 108 (7), 2421.
[31]. Moiseev, R. V.; Morrison, P. W.; Steele, F.; Khutoryanskiy, V. V., Penetration enhancers in ocular drug delivery. Pharmaceutics 2019, 11 (7), 321.
[32]. Proctor, C. M.; Chan, C. Y.; Porcarelli, L.; Udabe, E.; Sanchez-Sanchez, A.; del Agua, I.; Mecerreyes, D.; Malliaras, G. G., Ionic Hydrogel for Accelerated Dopamine Delivery via Retrodialysis. Chem. Mater. 2019, 31 (17), 7080.
[33]. Ruiz-Gatón, L.; Espuelas, S.; Huarte, J.; Larrañeta, E.; Martin-Arbella, N.; Irache, J. M., Nanoparticles from Gantrez® AN-poly (ethylene glycol) conjugates as carriers for oral delivery of docetaxel. Int. J. Pharm. 2019, 571, 118699.
[34]. Alruwaili, N. K.; Zafar, A.; Imam, S. S.; Alharbi, K. S.; Alotaibi, N. H.; Alshehri, S.; Alhakamy, N. A.; Alzarea, A. I.; Afzal, M.; Elmowafy, M., Stimulus Responsive Ocular Gentamycin-Ferrying Chitosan Nanoparticles Hydrogel: Formulation Optimization, Ocular Safety and Antibacterial Assessment. Int. J. Nanomed. 2020, 15, 4717.
[35]. Basu, A.; Domb, A. J., Ion Exchange Nanoparticles for Ophthalmic Drug Delivery. Bioconjugate Chemistry 2020, 31 (12), 2726-2736.
[36]. Yetisen, A. K.; Jiang, N.; Castaneda Gonzalez, C. M.; Erenoglu, Z. I.; Dong, J.; Dong, X.; Stoßer, S.; Brischwein, M.; Butt, H.; Cordeiro, M. F.; Jakobi, M.; Hayden, O.; Koch, A. W., Scleral Lens Sensor for Ocular Electrolyte Analysis. Adv. Mater. 2020, 32 (6), 1906762.