International Journal of Pharmacy and Pharmaceutical Sciences

ISSN- 0975-1491 Vol 9, Issue 9, 2017

Original Article

ORAL GENTAMICIN PREPARATION USING SOLIDIFIED LIPID PARTICULATE DELIVERY SYSTEM

MUSILIU ADEDOKUN*[1], TENDERWEALTH JACKSON[1], KELECHI UCHEGBU[2], ANTHONY ATTAMA[2]

[1]Department of Pharmaceutics and Pharmaceutical Technology, Faculty of Pharmacy, University of Uyo, Uyo, Nigeria, [2]Department of Pharmaceutics, Faculty of Pharmaceutical Sciences, University of Nigeria, Nsukka, Nigeria
Email: mo_adedokun@yahoo.com

Received: 18 Apr 2016 Revised and Accepted: 13 Jul 2017

ABSTRACT

Objective: Despite the broad pharmacological activity of gentamicin against a number of bacteria, it's very inadequate oral bioavailability due to poor intestinal membrane permeability has limited its formulation into oral dosage delivery system. This work was thus aimed at formulation and evaluation of gentamicin-loaded microemulsions based on preparation of lipid matrix for sustained release delivery.

Methods: Oral gentamicin suspensions were prepared by emulsification method using Tween 80 as a mobile surfactant in the lipid matrix dispersion. The resultant oral suspensions were evaluated for mean particle size and morphology using a photomicrograph, encapsulation efficiency/entrapment, EE (%), dispersibility, pH and absolute drug content. Release study as a function of inhibition zone diameter (IZD) and *in vitro* release study was also carried out. The *in vitro* release study was performed in both simulated gastric fluid (pH 1.2) and simulated intestinal fluid (pH 7.2) respectively. The release data were analyzed mathematically according to zero order, first order and Higuchi equations.

Results: The prepared suspensions were cream-white in colour, easily dispersed and well homogenized. Batch D, which had least amount of excipients incorporated into the lipid matrix showed clumped irregular-shaped and less free-flowing particles. The particle size was significantly influenced by lipid matrix combination ratio in the presence of a surfactant ($p<0.05$). The mean particle size diameters of the samples were 15.44 mm, 10.64 mm, 4.12 mm, and 2.70 mm for batches A, B, C and D respectively. The values of EE obtained varied between 47% and 59% with Batch B exhibiting the highest value. The Higuchi model gave the best release kinetics result followed by zero order kinetics.

Conclusion: Oral gentamicin prepared exhibited antibacterial properties against *Klebsiella spp., Escherchia coli, Bacillus subtilis, Staphylococcus aureus,* and *Pseudomonas aeruginosa.* The results suggest that a lipid matrix system could be useful as a sustained release oral delivery system of a poorly absorbable drug such as gentamicin.

Keywords: Lipid matrix, Gentamicin, Controlled release, Entrapment efficiency

DOI: http://dx.doi.org/10.22159/ijpps.2017v9i9.12278

INTRODUCTION

Gentamicin sulphate is an aminoglycoside antibiotic commonly used topically in the control of severe Gram positive and Gram negative microbial infections especially in burns and wounds as well as for treating bone and soft tissue infections [1]. It is a polarized water-soluble compound having very poor intestinal membrane permeability resulting in low oral bioavailability [2].

Despite its benefits, bacterial membrane barriers and adverse effects such as nephrotoxicity, ototoxicity and neurotoxicity due to extended use had limited gentamicin daily dosage [3, 4]. A lot of researchers had employed various assay methods for determining some aminoglycosides including gentamicin in different delivery systems. These include: microbiological [5], polarographic [6], chemiluminescence [7], capillary electrophoresis [8], immunoassay [9], thin layer chromatographic [10], high performance liquid chromatographic [11], spectrofluorimetric [12], and spectrophotometric [13, 14] methods.

Efforts had been made to determine the drug's optimal therapeutic regimens in order to increase its overall efficacy while minimizing drug toxicity. These include; use of labrasol [1], liposomes [15], solidified reverse micellar drug delivery systems [16-18], and hydrogels [19, 20]. Gentamicin transdermal microgels had also been prepared by Nnamani *et al.* in 2013 [21]. Also, in 2013, gentamicin-gold nano spheres for antimicrobial drug delivery to Staphylococcal infected foci were formulated by Ahangari *et al.* [22]. Microsphere-gentamicin formulated by some workers was found to be effective as potential drug carrier which could be employed for treatment of *E. coli* K88 infection [23]. Microsphere formulations of gentamicin using bovine serum albumin (BSA) and glutaraldehyde as a polymer matrix and cross-linker respectively were prepared by Haswani *et al.* The products exhibited a significant increase in bioavailability which would permit a reduction in the frequency of gentamicin administration and would effectively reduce the drug's dose related side effects [4].

Quite a number of workers had employed various formulation technologies including **s**elf-micro-**e**mulsifying delivery **s**ystems (SMEDDS) for delivery of some drugs like gentamicin, however, there seems to be no reported study on the use of the latter to achieve controlled the release of gentamicin and at the same time, evaluate its potentiality against different classes of microbes. This has, therefore, prompted us to formulate and evaluate gentamicin-loaded microparticles incorporated into lipid matrix formulation and surfactant combination with a view to achieving sustained release to enhance the intestinal permeability of gentamicin to achieve an improved antimicrobial activity.

MATERIALS AND METHODS

Materials

The materials used were gentamicin, phospholipon 90g and polysorbate 80 (tween 80) purchased from Williams and sons Ltd, England, beeswax and dibasic potassium phosphate (BDH Chemicals), distilled water (Lion Water, University of Nigeria, Nsukka) and goat wax. The latter was extracted from goat fat purchased from the local market, placed in a pot and allowed to melt at 60-80 °C and subsequently allowed to cool. Other chemicals employed were of laboratory grade.

Methods

Preparation of gentamicin-loaded microemulsions based on formulation of lipid matrix

Microemulsion loaded with gentamicin was prepared according to the formula in table (1). The lipid microparticles were

prepared using 1:1 (w/w) lipid matrices by a hot-emulsion technique using mixer followed by cooling at room temperature [24]. Four batches of SMEDDS were prepared for each lipid matrix according to the concentration of the gentamicin loaded (table 2). The lipid matrix incorporated progressively reduced as the drug component is increased. In each case, the lipid matrix was melted at 60 °C in a crucible, and the appropriate amount of gentamicin (for the loaded formulations) incorporated in sufficient volume of distilled water and brought to the same temperature with the lipid melt. The hot aqueous phase was poured into the melted lipid under high shear mixing using the mixer to give an o/w emulsion. The lipid microparticles suspension was obtained after cooling at room temperature for each lipid matrix ratio.

Table 1: Formula for preparation of gentamicin-loaded microspheres

Ingredients	Amount
Lipid matrix	10 %
Gentamicin	0, 1, 3, 5 %
Tween 80	1 %
Waterto	50 g

Table 2: Formulation of lipid matrix

Batch number	Tween 80	Drug (g)	% composition (w/w) bees wax+goat wax	Phospholipid	Water to
A	0.25	0.0	3.5	1.5	50g
B	0.25	0.5	3.5	1.5	50g
C	0.25	1.5	3.5	1.5	50g
D	0.25	2.5	3.5	1.5	50g

Characterization of the lipid microparticles

Determination of pH

A pH meter (Kent Industrial Measurements, England) was used to determine the pH of microparticulate suspension from each batch on weekly basis for 3 mo and the average values computed.

Determination of absolute drug content

The method used by Tahami *et al.* [25] was employed to evaluate the absolute drug content of the microparticles. A 0.5 g quantity of each batch of the suspended particles was placed in a 100 ml volumetric flask. The flask was made up to volume with distilled water and allowed to equilibrate at room temperature with intermittent shaking. This gave the stock solution. Nine solution batches having the following concentrations: 10 mg %, 20 mg %, 30 mg %, 40 mg %, 50 mg %, 60 mg %, 70 mg %, 80 mg %, 90 mg %, were made by diluting 10, 20, 30, 40, 50, 60, 70, 80, 90 ml of the stock solution to 100 ml with distilled water. The corresponding absorbance of each of the solutions was obtained with a UV spectrophotometer (Jenway 6305 Spectrophotometer) at 370 nm wavelength. The Beer-Lambert's plot was obtained from the results.

Determination of EE (%)

The values of EE (%) were determined by the method described by some researchers [26-28]. The theoretical drug content in the suspension was compared with the actual amount of the drug obtained from the drug content studies to get EE (%). This was calculated using the equation [26]:

$$\text{EE (\%)} = \frac{\text{Real Drug Loading (RDL)}}{\text{Theoretical Drug Loading (TDL)}} \times 100$$

Preparation of simulated gastric fluid (SGF)

SGF was prepared by dissolving sodium chloride in concentrated hydrochloride acid, mixing it properly and the volume made up to 1 litre with distilled water and the pH adjusted to 1.2 [29].

Preparation of simulated intestinal fluid (SIF)

SIF was prepared by dissolving 6.8 g of monobasic potassium phosphate in 250 ml of distilled water, mixed well followed by the addition of 77 ml, of 0.2 N sodium hydroxide and 500 ml of distilled water. This was mixed and made up to 1.0 l with distilled water and the pH adjusted to 7.2 [29].

Release study of gentamicin-loaded suspension

Beer's plot was obtained at the following concentrations: 0.2, 0.4, 0.6, 0.8, 1.0 mg/ml for gentamicin in SGF at 341 nm. The USP XXII rotating paddle apparatus (Erweka germany) was used in the release study [27, 28, 30]. The dissolution medium consisted of 250 ml of freshly prepared SGF (pH 1.2) maintained at 37.1 °C. Dialysis as described by previous workers [24] was employed. A 0.5 g quantity of the formulated suspension was placed in the membrane and each securely tied with a thermo-resistant thread and then placed in the dissolution medium. The paddle at 100 rpm provided agitation. At predetermined time intervals, 5.0 ml portions of the dissolution medium were withdrawn, and their absorbance determined using the spectrophotometer above a wave length of 341 nm. The dissolved volume of dissolution medium was kept constant by replacing with 5 ml of the fresh medium after each withdrawal to maintain sink condition. The amount of drug released at each time interval was determined with reference to the standard Beer's plot for the drug in SGF. Release study was also similarly carried out in SIF.

Release study as a function of IZD

The agar diffusion method [24] was used in the determination of the IZD (mm) of the gentamicin-loaded lipid microparticles dispersion. Seeded agar plate was prepared by incorporating the specific microorganism and molten nutrient agar subsequently. It was left to stand until the seeded agar solidified. A cork borer of 8 mm diameter was used to bore holes at four ends of the seeded agar. The different gentamicin suspension batches were placed into the holes formed. The plate was carefully covered and incubated for 24 h. The microorganisms employed include *Klebsiella spp, E. coli, B. subtilis, S. aureus,* and *P. aeruginosa* (obtained as clinical isolates from the Pathology department of the University of Nigeria Teaching Hospital, Enugu, Nigeria). The determination was done in triplicates.

Determination of particle size and morphology

Particle size and morphology of the microparticles were determined by digital microscopy [26]. A 5 mg quantity of suspension was placed on a microscope slide. The slide was covered with a cover slip and observed using image-guided lens under a photomicroscope at a magnification of x 1000. Different particles from the suspension showing different orientations were measured and the mean values were taken.

Centrifugation

In order to estimate metastable system, the optimized lipid micro particles formulation was diluted with purified distilled water. The suspension was centrifuged at 3000 rpm for 15 min at 25 °C and observed for any change in homogeneity of the formulation.

Statistical analysis

All the experiments were carried out in triplicates (that is, n = 3). The data obtained were subjected to statistical analysis using a one-

way analysis of variance (ANOVA) followed by Fisher (least significant difference) multiple comparison procedures to evaluate significant differences between groups. The differences were considered significant at $p<0.05$.

RESULTS AND DISCUSSION

The microparticles formed were spherical in shape and cream white in colour. Batch A which contained no drug showed very orderly and free-flowing particles. Batches B-D, with progressively decreased lipid matrix incorporated, showed clumped, irregular-shaped and less free-flowing particles. The mean particle dimensions of the batches A, B,C and D, as presented in table (3) also reduces in that order. As the drug content increased (that is, as the lipid matrix component decreased), the mean particle diameter also decreased. This direct influence of the lipid matrix on mean particle diameter is statistically significant ($p<0.5$). It was also observed that the free-flow properties of all the batches of suspension were maintained at room temperature. It can, therefore, be inferred that the particle morphology and flow characteristics of the formed microparticles are influenced by the relative proportion of the lipid matrix content similar to earlier reported cases [17, 24]. The average pH values obtained were 6.92±0.22, 6.87±0.15, 7.01±0.18 and 6.95±0.09, for batches A–D, respectively. Statistically, there was no significant change in the values across the batches over a three months storage time ($p>0.05$). This indicates that during this storage time, there was no notable decomposition of any of the constituents of the preparations [12, 31]. This is an affirmation of the stability of the formulations.

EE (%) was expressed as the percentage of the total amount of gentamicin used initially and the values are shown in table (3). The value of EE for gentamicin suspension per-batch was highest with batch B (59%). This can be attributed to a greater amount of drug incorporated into the lipid matrix which increases the diameter of the microparticles and EE by increasing the core available for entrapping a large amount of drug [26]. Statistically, the difference between EE values among the batches was significant ($p<0.5$).

The presence of phospholipon 90G and polysorbate 80 in the suspensions increased their entrapment efficiency. While the latter component, being a hydrophilic surfactant promoted the solubilization of gentamicin within the core lipid matrix, the former gave rise to the formation of structured lipid matrices, which improved the entrapment of the drug in the core of the preparations. [24, 32]. The increase observed in the formulations is suggestive of their possible employment as sustained release delivery system.

Table 3: Values of mean particle dimensions and EE (%) for all the SMEDDS batches

Sample batch	Mean particle size diameter (µm)	Perimeter (µm)	Area (µm²)	EE (%)
A	15.44	49.05	184.59	-
B	10.64	34.08	89.65	59
C	4.13	13.29	14.08	52
D	2.71	8.71	6.05	47

n = 3; the presented results are the average of three (3) determinations

When infinite dilution is done to the formulation, there is the possibility of phase separation, as microemulsions are formed at a particular concentration of oil, surfactant and water. For oral formulations, the process of dilution by the GI fluid will result in the gradual desorption of surfactant located at the global interface. The process is thermodynamically driven by the requirement of surfactant to maintain an aqueous phase concentration equivalent to its critical micelle concentration (CMC). In the present investigation (dispersibility test), distilled water was used as a dispersion medium because it is widely reported that there is no significant difference in the formulation prepared using nonionic surfactants, dispersed in either water, SGF or SIF [33-35].

Formulations B and C containing 0.5% and 1.5% respectively passed the thermodynamic stability test whereas formulation D containing 2.5% did not pass the test as shown in the table (4). This may possibly be due to insufficient lipid matrix in the latter formulation, suggesting that the lipid possesses the ability to stabilize the preparation.

Table 4: Results of thermodynamics stability test

Suspension batch	% Drugs concentration	Centrifugation test	Inference
A	0.0%	✓	PASSED
B	0.5%	✓	PASSED
C	1.5%	✓	PASSED
D	2.5%	✓	FAILED

n = 3; the presented results are the average of three (3) determinations

Sink conditions are often violated when using conventional release method for dispersed systems. So, the method must be developed for lipid microparticles to separate the dissolved drugs from micro-emulsion associated drugs before their determination. It has been reported that a dialysis method has been applied to gentamicin lipid microparticles, and a relatively high release rate was obtained in this study, a bulk-quilibrium reversed dialysis bag method was developed to allow an increase in the membrane surface area available for transport from the donor to the phase of the receiver and hence, to maintain sink condition in the donor phase by infinite dilution of the medium in the outer vessel. The small particle size of the microparticles also probably contributed to the increased release rate.

Fig. (1) Represents the typical drug release plots from the dispersion for the different optimization variables. The degree and the mode of release of gentamicin from the prepared microparticles were analyzed mathematically by fitting the dissolution data into different kinetic models: zero order; first order, Higuchi's equations, and coefficient of correlation (r^2) values were calculated for the linear curves by regression analysis of the plots [28]. In SIF the data were best fitted to Higuchi equation. Batch D (containing 2.5% gentamicin), **b**atch C (1.5% gentamicin), and **b**atch B (0.5% gentamicin), exhibited r^2 values of 0.940, 0.932 and 0.824, respectively.

In SGF, the data were best fitted to Higuchi for batch D containing 2.5% gentamicin with r^2 value of 0.985. Batch B containing 0.5% gentamicin had r^2 value of 0.984 while batch C containing 1.5% gentamicin had r^2 value of 0.967. After incubating the seeded plate containing gentamicin samples for 24 h, the plates were observed and the IZD were measured planimetrically. It was observed that even in the absence of gentamicin, the microorganisms were inhibited (table 5). This implies that some of the excipients could exhibit some antibacterial activity.

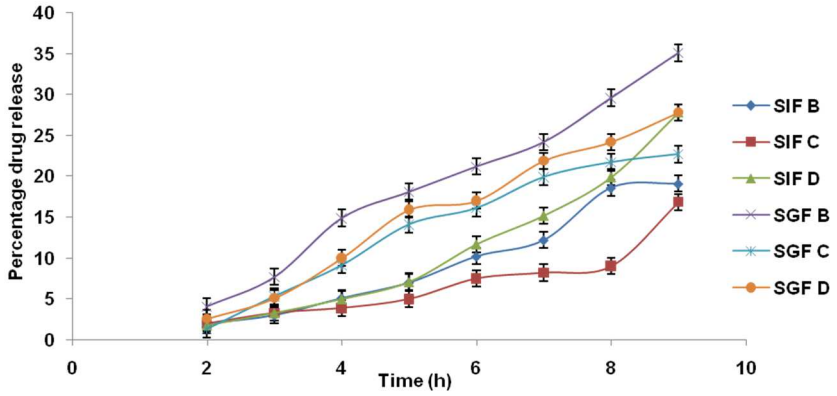

Fig. 1: Release profile of gentamicin from the microparticles in SIF and SGF, n = 3; the presented results are the average of three (3) determinations

Table 5: Values of IZD for all the gentamicin preparations

Microbes	Gentamicin preparations and their IZD values							
	Batch D		Batch C		Batch B		Batch A	
	IZD (mm)	Mean IZD (mm)	IZD (mm)	Mean IZD (mm)	IZD (mm)	Mean IZD (mm)	IZD (mm)	Mean IZD (mm)
Klebsiella sp	40.00		43.00		28.00		17.00	
	30.00		41.00		28.00		16.00	
	35.00	35.00	40.00	41.30	30.00	28.66	17.00	16.66
E. coli.	36.00		5.00		30.00		14.00	
	37.00		35.00		30.00		14.00	
	36.00	36.33	36.00	35.33	28.00	29.33	14.00	14.00
B. subtilis	30.00		29.00		26.00		20.00	
	32.00		28.00		26.00		20.00	
	30.00	30.66	30.00	29.00	27.00	26.33	23.00	21.00
S. aureus	38.00		36.00		33.00		21.00	
	36.00		38.00		31.00		22.00	
	38.00	37.33	35.00	36.33	30.00	31.30	22.00	21.66
P. aeruginosa	45.00		45.00		37.00		20.00	
	45.00	45.00	45.00	44.60	37.00	37.30	20.00	19.66
	45.00		44.00		38.00		19.00	

n = 3; the presented results are the average of three (3) determinations

From table (5), it can be seen that batch D had the highest activity and against *P. aeruginosa.* This expectedly shows that the higher the gentamicin incorporated, the greater the antibacterial activity. The result of the IZD measurement as presented in table (5) is in agreement with earlier findings that the quantity of drug loaded into the lipid matrix is directly proportional to the IZD produced [24, 31]. Statistically, the pharmacological effects exhibited on the microbes by different batches of the formulation vary significantly ($p<0.05$). From the result obtained, it can be inferred that lipid micro particulate suspensions prepared by SMEDDS using optimized variables have antibacterial properties on the organisms.

CONCLUSION

From this study, the higher the lipid matrix incorporated the higher the particle size diameter as well as EE (%). Furthermore, the critical process in the preparation by the self-micro-emulsifying gentamicin suspension played an important role in the *in vitro* drug release. It was shown that the release of gentamicin from dispersion followed zero order and Higuchi release kinetics rather than first order release. Sustained release gentamicin suspension can be prepared using the above-stated optimization variables as an increase in the concentration of the lipid matrix would increase the tendency of its particle entrapment.

ACKNOWLEDGEMENT

The authors are grateful to management and staff of God's Glory Computers Institute, Uyo, technical staff of Department of Pharmaceutics, University of Nigeria, Nsukka and of the Pathology Department, University of Nigeria Teaching Hospital, Enugu, Nigeria.

AUTHORS' CONTRIBUTION

This work was carried out in collaboration between all the four authors in the concept and design of the work, collection, assembly, analysis and interpretation of data, writing, critical revision and approval of the final manuscript.

CONFLICT OF INTERESTS

Declared none

REFERENCES

1. Nnamani PO, Kenechukwu FC, Anugwolu CL, Obumneme AC, Attama AA. Characterization and controlled release of gentamicin from novel hydrogels based on poloxamer 407 and polyacrylic acids. Afr J Pharm Pharmacol 2013;7:2540-52.
2. Rama Prasad YV, Eaimtrakarn S, Ishida M, Kusawake Y, Tawa R, Yoshikawa Y, *et al.* Evaluation of oral formulations of gentamicin containing labrasol in beagle dogs. Int J Pharm 2003;11:13-21.
3. Robert MS, Walters KA. Dermal absorption and toxicity assessment. New York (USA): Marcel Dekker; 1998. p. 321-2.
4. Haswani DK, Nettey H, Oettinger C, D'Souza MJ. Formulation, characterization and pharmacokinetic evaluation of gentamicin sulphate loaded albumin microspheres. J Microencapsul 2006;23:875-86.

5. Yamamoto CH, Pinto TJ. Rapid determination of neomycin by a microbiological agar diffusion assay using triphenyl tetrazolium chloride. J AOAC Int 1996;79:434-40.
6. Liang Y, Zhang T. Quantitative determination of streptomycin by first-derivative high-speed pulse polarography. Zhongguo Kangshengsu Zazhi 1991;16:102-5.
7. Yang CY, Zhang ZJ, Wang JL. New luminal chemiluminescence reaction using diperiodatoargentate as oxidate for the determination of amikacin sulphate. Luminescence 2010;25:36-42.
8. Huidobro AL, Garcia A, Barbas C. Rapid analytical procedure for neomycin determination in ointments by CE with direct UV detection. J Pharm Biomed Anal 2009;49:1303-7.
9. Sánchez-Martínez ML, Aguilar-Caballos MP, Gómez-Hens A. Long wavelength homogeneous enzyme immunoassay for the determination of amikacin in water samples. Talanta 2009;78:305-9.
10. Kaya SE, Filazi A. Determination of antibiotic residues in milk samples. Kafkas Universitesi Veteriner Fakultesi Dergisi 2010;16:31-5.
11. Bohm DA, Stachel CS, Gowik P. Confirmatory method for the determination of streptomycin in apples by LC-MS/MS. Anal Chim Acta 2010;672:103-6.
12. El-Shabrawy Y. Fluorimetric determination of aminoglycoside antibiotics in pharmaceutical preparations and biological fluids. Spectrosc Lett 2002;35:99-109.
13. Al-Sabha TN. Spectrophotometric determination of amikacin sulphate via charge transfer complex formation reaction using tetracyanoethylene and 2,3-dichloro-5,6 dicyano-1,4-benzoquinone reagents. Arabian J Sci Eng 2010;35:27-40.
14. Omar MA, Nagy DM, Hammad MA, Aly AA. Validated spectrophotometric methods for determination of certain aminoglycosides in pharmaceutical formulations. J Appl Pharm Sci 2013;3:151-61.
15. Jia Y, Joly H, Omri A. Liposomes as a carrier for gentamicin delivery: development and evaluation of the physicochemical properties. Int J Pharm 2008;359:254-63.
16. Umeyor CE, Kenechukwu FC, Ogbonna JDN, Builders PF, Attama AA. Preliminary studies on the functional properties of gentamicin in SRMS-based solid lipid microparticles. Int J Drug Delivery Technol 2011;1:130-42.
17. Umeyor CE, Kenechukwu FC, Ogbonna JDN, Chime SA, Attama AA. Preparation of novel solid lipid microparticles loaded with gentamicin and its evaluation *in vitro* and *in vivo*. J Microencapsul 2012;29:296-307.
18. Umeyor CE, Kenechukwu FC, Ogbonna JDN, Chime SA, Attama AA. Investigation of solidified reverse micellar systems as novel carriers for oral delivery of gentamicin. J Pharm Res 2014;5:4914-20.
19. Changez M, Burugapalli K, Koul V, Choudhary V. The effect of the composition of poly (acrylic acid)-gelatin hydrogel on gentamicin sulphate release: *in vitro*. Biomaterials 2003;24:527-36.
20. Eljarrat-Binstock E, Raiskup F, Stepensky D, Domb AJ, Frucht-Pery J. Delivery of gentamicin to the rabbit eye by drug-loaded hydrogel iontophoresis. Invest Ophthalmol Visual Sci 2004;103:1-12.
21. Nnamani PO, Kenechukwu FC, Dibua EU, Ogbonna CC, Monemeh UL, Attama AA. Transdermal microgels of gentamicin. Eur J Pharm Biopharm 2013;84:345-54.
22. Ahangari A, Salouti M, Heidari Z, Kazemizadeh AR, Safari AA. Development of gentamicin-gold nano spheres for antimicrobial drug delivery to staphylococcal infected foci. Drug Delivery 2013;20:34-9.
23. Sarabia-Sainz A, Montfort GR, Lizardi-Mendoza J, Sánchez-Saavedra MP, Candia-Plata MC, Guzman RZ, *et al.* Formulation and characterization of gentamicin-loaded albumin microspheres as a potential drug carrier for the treatment of E. coli K88 infections. Int J Drug Delivery 2012;4:209-18.
24. Momoh MA, Esimone CO. Phospholipon 90H (P90H)-based PEGylated microscopic lipospheres delivery system for gentamicin: an antibiotic evaluation. Asian Pacific J Trop Biomed 2012;2:889-94.
25. Al-Tahami K. Preparation, characterization, and *in vitro* release of ketoprofen loaded alginate microspheres. Int J Appl Pharm 2014;6:9-12.
26. Abraham S, Abhilash TV**,** Jacob L. Formulation and evaluation of perindopril microcapsules using different polymer. Asian J Pharm Clin Res 2017;10:153-6.
27. Kalita B, Saikia K, Kalita B. Development and characterization of the mucoadhesive microsphere-loaded intranasal gel of venlafaxine hydrochloride. Asian J Pharm Clin Res 2016;9:139-44.
28. Deshmukh MT, Mohite SK. Formulation and characterization of olanzapine-loaded mucoadhesive microspheres. Asian J Pharm Clin Res 2017;10:249-55.
29. Adikwu MU, Nnamani PO, Attama AA. Evaluation of snail mucin as bioadhesive agent for the delivery of chlorpropamide. Biol Res 2005;3:75-85.
30. Mohite PB, Khanage SG, Harishchandre VS, Shirsath Y. Recent advances in micro sponges drug delivery system. J Crit Rev 2016;3:9-16.
31. Kenechukwu FC, Umeyor CE, Momoh MA, Ogbonna JDN, Chime SA, Nnamani PO, *et al.* Evaluation of gentamicin-entrapped solid lipid microparticles formulated with a biodegradable homolipid from *Capra hircus*. Trop J Pharm Res 2014;13:1199-205.
32. Attama AA, Okafor CE, Builders PF, Okorie O. Formulation and *in vitro* evaluation of a PEGylated microscopic lipospheres delivery system for ceftriaxone sodium. Drug Delivery 2009;16:448-57.
33. Fana Y, Lia X, Zhoua Y, Fana C, Wanga X, Huangb Y, *et al*. Improved intestinal delivery of salmon calcitonin by water-in-oil microemulsions. Int J Pharm 2011;416:323-30.
34. Hanh ND, A Mitrevej, Sathirakul K, Peungvicha P, Sinchaipanid N. Development of phyllanthin-loaded self-micro emulsifying drug delivery system for oral bioavailability enhancement. Drug Dev Ind Pharm 2015;41:207-17.
35. Kollipara S, Gandhi RK. Pharmacokinetic aspects and *in vitro–in vivo* correlation potential for lipid-based formulations. Acta Pharm Sinica B 2014;4:333-49.

How to cite this article

- Musiliu Adedokun, Tenderwealth Jackson, Kelechi Uchegbu, Anthony Attama. Oral gentamicin preparation using solidified lipid particulate delivery system. Int J Pharm Pharm Sci 2017;9(9):22-26.