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FORMULATION AND EVALUATION OF NANOGEL CONTAINING *ALOE BARBADENSIS*

Deepak Koshti [1], Dr.Richa Mishra [2]

[1]Research Scholar, Sunrise University, Alwar

[2] Professor, Sunrise University, Alwar

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Address for Correspondence: Deepak Koshti

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Abstract

Nanogels are promising and innovative drug delivery system that can play a vital role by addressing the problems associated with old and modern therapeutics such as nonspecific effects and poor stability. Nanogels appear to be excellent candidates for brain delivery. One future goal of research in this area should be the improved design of microgels/nanogels with specific targeting residues to enable highly selective uptake into particular cells. In this study an attempt was made to prepare and evaluate Nanogel of containing *Aloe barbadensis.*

Keywords: Nanogel, *Allium cepa,* drug release, particle size, drug entrapment efficiency

INTRODUCTION

The term 'nanogels' defined as the nanosized particles formed by physically or chemically crosslinked polymer networks that is swell in a good solvent. The term "nanogel" (NanoGel™) was first introduced to define cross-linked bifunctional networks of a polyion and a nonionic polymer for delivery of polynucleotides (cross-linked polyethyleneimine (PEI) and poly (ethylene glycol) (PEG) or PEG-cl-PEI) (Kabanov and Vinogradov, 2008). Sudden outbreak in the field of nanotechnology have introduced the need for developing nanogel systems which proven their potential to deliver drugs in controlled, sustained and targetable manner. With the emerging field of polymer sciences it has now become inevitable to prepare smart nano-systems which can prove effective for treatment as well as clinical trials progress. (Dorwal et al., 2012)

MATERIALS AND METHOD

Drug Combination Study of *Aloe barbadensis* in Nanogel

Preparation of CDI-activated Pluronic F127

A solution of Pluronic F127 (1.25 g, 0.1 mmol) in anhydrous THF (15 mL)was added dropwise (during 2 hr.) to an excess amount of CDI (0.81 g, 5 mmol) in THF (15 mL) at room temperature under nitrogen atmosphere. After the addition, the mixturewas kept stirring for an additional 6 hr. The solution was concentrated to a small volumeunder vacuum and poured into ethyl ether (150 mL), and the precipitate was collected by filtration to get CDI-activated Pluronic F127. This process was repeated three times to remove the unreacted CDI. The CDI-activated Pluronic F127 was obtained as white powder after drying under vacuum at room temperature for 12 hr.

Preparation of F127/PEI nanogel

The F127/PEI nanogel was prepared by an emulsification/solvent evaporation method. The activated Pluronic F127 were dissolved in chloroform and added drop- wise to an aqueous solution of PEI under stirring. The mixture was sonicated for 3min and theorganic solvent in the emulsion was removed by rotary vacuum evaporation at 50°C for 45 min. The remaining

solution was centrifuged at 3000 rpm for 30 min to remove adhesive fragments. After neutralizing with hydrochloric acid, the solution was dialyzed in a dialysis bag with 14,000 – 16,000 Da molecular weight cut-off against water at pH 4.0. The purified nanogel samples were freeze dried to obtain F127/PEI nanogel.

Drug loading

The drug (freeze dried *Aloe barbadensis* powder and ethanol extract powder of *Aloe barbadensis* gel in combination) and lyophilized empty nanogels were dissolved separately in mixture of methanol and water (1:1), and then both were mixed, and the solvent was subsequently removed by rotary vacuum evaporation. The resulting film formed was further hydrated with a suitable amount of phosphate buffered saline pH 7.4.

Table 1: Formulation Table

Batch	Drug Combination Ratio (DCR)	Concentration of Pluronic F127 (mg)	Concentration of PEI (mg)	Water (ml)	Chloroform (ml)
G1	1.032	100	100	20	2
G2	1.032	200	100	20	2
G3	1.032	300	100	20	2
G4	1.032	100	200	20	2
G5	1.032	200	200	20	2
G6	1.032	300	200	20	2
G7	1.032	100	300	20	2
G8	1.032	200	300	20	2
G9	1.032	300	300	20	2

Note: Each batch of nanogel formulation contains ~1% of active constituent in the form of combination of crude drug.

Evaluation of Optimized Nanogel

pH: The pH of nanogel formulation was determined using digital pH meter as per the method described in Indian Pharmacopoeia (2007). Before measuring the pH of optimized formulation, the pH meter was calibrated with the phosphate buffer pH 4.0, 7.0 and 9.0. Then nanogel was taken in a small glass beaker and the electrode of pH meter was dipped into it for a minute and the pH was noted. The measurement of pH of each formulation was done in triplicate and mean values were calculated. (Shah K 2012)

Viscosity: The viscosity of the prepared formulations was determined using Brookfield viscometer as the method described by shah et al. (2012). The selected formulations were poured into the sample adaptor of the viscometer. The viscosity was measured at 10 min after the rotation of the spindle. The viscosity measurements were made in triplicate.

Particle Size: The particle size of the optimized nanogel was measured using malvern zeta sizer. (Islam P et al 2016)

Drug Entrapment Efficiency: Drug entrapment efficiency of optimized nanogel was measured as per the method described in section 9.4.4.

***In-vitro* Release Study:** *In vitro* drug release study of optimized nanogel was performed as per the method described in section 9.4.6.

RESULTS AND DISCUSSION

Table 2: ***In-vitro*** **drug release profile of nanogel formulations of batches G1- G9**

% CDR									
Time (hr.)	**0.5**	**1**	**2**	**3**	**4**	**6**	**8**	**10**	**12**
G1	11.44	26.25	49.97	59.49	62.99	78.61	84.59	90.22	94.62
G2	**10.01**	**15.65**	**22.41**	**30.90**	**35.66**	**52.46**	**64.76**	**79.93**	**95.46**
G3	11.83	18.66	26.45	35.97	41.15	57.63	69.20	82.90	94.88
G4	12.71	24.74	35.41	45.86	50.68	64.21	72.59	82.69	92.35
G5	13.55	28.43	51.86	63.00	64.01	79.76	86.17	90.00	93.73
G6	10.03	21.50	32.22	40.88	45.26	59.60	69.54	81.97	93.12
G7	10.87	27.48	44.84	56.00	59.96	72.55	79.57	85.75	92.67
G8	11.65	26.92	42.79	53.90	55.46	68.15	74.57	82.74	94.26
G9	10.75	25.96	50.08	58.87	62.07	76.69	84.12	90.86	94.77

pH

The pH of optimized nanogel was determined using digital pH meter. The optimized formulation of nanogel had pH **5.41 ± 0.0142 (n=3)**, which is like the pH of skin i.e.,4 – 7.

Viscosity

The viscosity of optimized nanogel was determined using Brookfield viscometer. Using spindle, no S63 at 100 rpm, the viscosity of optimized nanogel formulation was found to be **2.78 ± 0.09 (n=3)**. As the concentration of polymer solution increases viscosity also increases.

Particle size

The particle size of optimized nanogel was measured by using Malvern zeta sizer. Particle size of optimized nanogel was found to be **86.07 ± 0.15 nm (n=3)** which is desired for the nanogel.

Drug entrapment efficiency

Drug loaded amount of optimized nanogels was measured by HPLC after centrifugation at 12,000 rpm for 10 min. The % entrapped drug in optimized nanogel was found to be 75.06 ± 1% (n=3).

In-Vitro **Drug Release profile**

In-vitro drug release study of optimized nanogel was performed using Franz diffusion cell. From the release study, it was found that optimized nanogel shows initial burst release of drug in first half hours and afterward provides sustained release of drug. The optimized nanogel was shown release of more than 90 % (94.45%) of drug in 12 hr.

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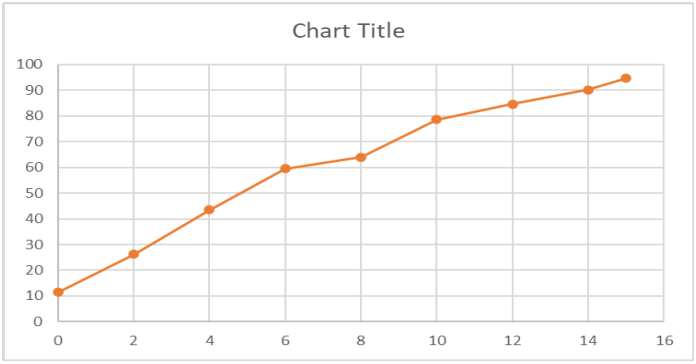

Figure 1: Drug release profile of optimized nanogel

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