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FORMULATION AND EVALUATION OF TRANEXAMIC ACID MICROSPONGES FOR TOPICAL DRUG DELIVERY SYSTEM

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ABSTRACT

Tranexamic acid it belong to a class of drugs known as antifibrinolytic, thereby preventing prolonged bleeding and slowing the breakdown of clots. the present study was taken to the development of topical drug delivery of formulation to the facilitate the controlled release of active drug into the skin, release of the drug into skin are controlled in manner and reduces the side effect or improved in the product efficiency. generally microsponges are mainly release of the drug and enhance the stability and effectively reduce the side effect of drug. Tranexamic acid loaded microsponges were prepared by using the Quasi-emulsion solvent diffusion method. having all nine formulation of tranexamic acid microsponges prepared by using polymer eudragit S100. Prepared microsponges were analyzed for the partical size, flow property of the microsponges, production yield, Drug loading efficiency, drug content and In-vitro drug release study. Microsponges are having a spherical in shape having a polymeric porous in nature.

KEYWORDS: topical drug delivery system, microsponges, tranexamic acid, polymeric porous, eudragit S 100.

INTRODUCTION

Tranexamic acid is in a class of medication also known as antifibrinolytic agent. It should be work to improve the blood clotting. Tranexamic acid belong to BCS classification of class I, it's meaning that showing high solubility and extended of permeation. Tranexamic acid is a hemostatic agent which is mainly acts in competitive inhibits activation of plasminogen, thereby reducing the conversion of plasminogen to plasmin which is required in formation of the blood clots. Which includes the procoagulant factors V and VIII. Tranexamic acid have a synthetic derivative of the amino acid lysine.[1] microsponges drug delivery system are controlled the drug release rate or drug targeted to the specific side of the body. It should be integrated to optimize the efficacy and cost effectiveness. Release and absorption of the drug is depend upon the characteristic of the drug. Microsponges are microscopic, polymeric and porous sponge like in nature. Microsponges having a non-collapsible microsphere having a large porous surface which is mainly use in a extended topical modified drug release.[2,3,4] Topical delivery is also called as the application of drug containing formulation of the skin or mucous membrane, to treat the specific cutaneous disorders (e.g.) or cutaneous manifestations of a generalized disease (e.g. psoriasis), with the intent of containing the pharmacological effect of the drug only to the surface or within the layer of skin or mucous membrane. The formulations are available in difference forms, like from solid through semisolid to liquid. Topical administration means application to the surfaces such as the skin or mucous membrane to treat ailments via a large classes including such as medicated powder, cream, foams, gel, lotions and ointment. Many topical medications are epicutaneous, meaning that they are applied directly to the skin.[5]

MATERIAL AND METHOD

Material

The formulation of tranexamic loaded microsponges having drug, excipients and chemicals were used for the formulation. Sample of tranexamic acid are was purchase from the Aarti pharma. Other excipient and chemical such as Eudragit S 100, PVA (polyvinyl alcohol), glycerol, and dicloromethane were obtained from research lab.

Formulation and development

Preparation of microsponges of tranexamic acid

Nine batches of microsponges are coded by F_1, F2, F3, F4, F5, F6, F7, F8, F9, utilizing different proportions of eudragit RS100 and polyvinyl alcohol phase (PVA) were prepared by emulsion solvent diffusion method. Microsponges prepared by using Quasi-emulsion solvent diffusion method. External phase are prepared by containing 200 ml of distilled water and 0.1 mg PVA (polyvinyl alcohol). Then internal phase are prepared, it consisted of tranexamic acid, polymer such as eudragit

S100 and dichloromethane. Eudragit are dissolved in dichloromethane and then drug are slowly added the polymeric solution in dissolved under the ultrasonication at 35^0c. glycerol which was added in amount of the 5ml of purpose of facilitated the plasticity. Inner phase are prepared and then added in the previously. Prepared external phase at room temperature. Then continuous stirring for 60 min. then the mixture filtered and isolated the microsponges then the washed and dried in vacuum oven for the 40°c for 1hrs.[6,7]

Table 1:- Formulas for Microsponges of tranexamic acid.

Sr. No.	Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	Tranexamic acid (gm)	1	1.2	2	1	1	1	2	2	2
2	Eudragit S 100(mg)	0.2	0.4	1gm	0.25	0.2	0.2	1gm	1gm	1gm
3	DCM (ml)	5	10	20	10	5	5	15	15	15
4	Glycerol (ml)	1	1	1.5	1	1	1	1.5	1	1.5
5	PAV (mg)	0.05	0.1	0.5	0.1	0.1	0.1	0.5	0.5	0.5
6	Water	200	200	200	200	200	200	200	200	200

Characterization of Microsponges

Micrometric property of microsponges[8-11]

Bulk density

To determination of the mass of powder divided by bulk volume of powder is also called as bulk density. Accurately weighted the 10 gm of sample powder which previously passed through 20# no. of sieve, then transferred in 50 ml of graduated cylinder. Cautiously level of the powder are without compacting and unsettled apparent volume is not down. To calculated the bulk density in gm/ml by the following equation.

$$bulk\ density = \frac{mass}{bulk\ volume}$$

Tapped density

To determination of the tapped density accurately weigh of sample powder and then transferred in 50 ml of the graduated measuring cylinder. Tap the cylinder are mechanically containing the sample and allowing it to fall under its own weight via tapped density apparatus. tapped the cylinder for 500 times and to determine by tapped density.

$$tapped\ density = \frac{weight\ of\ sample}{tapped\ volume}$$

Carr's index

The compressibility index of microsponges determination mainly by Carr's compressibility index. Evaluate the simple test of the bulk density and tap density of microsponges and rate at which packed down. Calculation of the Carr's index following formula was used.

$$carr's\ index\ (\%) = \frac{TD - BD}{TD} \times 100$$

Hausner's ratio

To determination of the hauser's ratio is a number that is correlated to the flow ability of the microsponges, formula for calculation of Hausner's ratio are following.

$$hausner's\ ratio = \frac{TD}{BD}$$

Angle of repose

The angle of repose are mainly used to determination of flow property of the powder. Placed in funnel was 2 cm above the horizontal surface. then powder sample are allowed to flow from the funnel, then pile of the powder was obtained, and diameter of pile was obtained and radius of pile was calculated.

Angle of repose is calculated by using equation

Angle of repose $0 = \tan^{-1}h/r$

Where,

0 = angle of repose

h = height of pile

r = radius of the pile

Determination of loading efficiency and production yield[12-14]

Determination of loading efficiency

A sample of dried microsponges equivalent to 10 mg was taken in mortar and pestle and add little amount of phosphate buffer of pH 6.8 and allowed to stand for 24 hours. Then transferred content in to 100 ml volumetric flask and make up volume to 100 ml with phosphate buffer of pH 6.8. The solution was filtered through whatmann filter paper. From the resulting solution take 1 ml in to 100 ml volumetric flask and then make up volume to 100 ml with phosphate buffer of pH 6.8. Drug content was determined by UV spectrophotometer at 239 nm. The entrapment was calculated by using following formula. The loading efficiency (%) of the microsponges can be calculated according to the following equation:

$$loading\ efficiency(\%) = \frac{actual\ drug\ in\ microsponges}{T\square erotical\ drug\ concentration} \times 100$$

Production yield

The production yield of the microsponges can be determined by calculating accurately the initial weight of the raw materials and the last weight of microsponges obtained.

$$Production\ yield\ (PY) = \frac{Practical\ mass\ of\ microsponges}{T\square erotical\ mass\ (Polymer + Drug)} \times 100$$

Size analysis of microsponges

The mean diameter of 100 dried microsponges was determined by optical Microscopy. The optical

microscope was fitted with a stage micrometer by which the size of microsponges could be determined.

Drug content

Microsponge equivalent to 100 mg of tranexamic acid microsponges were dissolved and made up to the mark in 100 mL volumetric flask with methanol, further 10 mL was diluted to 100 mL with methanol and the final dilution were using methanol to get concentration within beer's range. The absorbance was measured spectrophotomertically at 224.5 nm using blank microsponge treated in the same manner as sample.

In-vitro drug release study

In vitro release rate studies were carried out by paddle method specified in USP XXIII. Accurately weighted sample of microsponges were used which were calculated to contain 200 mg of tranexamic acid microsponges. They were placed in pH 7.4 phosphate buffer solution at 37± 1^0c and rotated at 100 rpm. Five ml aliquots were withdrawn at 5, 10, 15, 20, 30, 45, 60, 90, and 120 h and a last aliquot was withdrawn at 24 h. the sample were assayed at 262 nm.[15]

RISULT AND DISCUSION

Result

Characterization of tranexamic acid

Preformulation Studies

Table 2: Observation for Preformulation Studies.

Parameter	Standard	Result
Melting point	386-392^{0}c	384-390^{0}c
Solubility	Soluble in water, glacial acetic acid, very slightly soluble in alcohol, ether	Soluble in water
Colour	White crystalline powder	White powder

Micrometrics property of microsponges

Table 3: Observation of Micrometrics Property of Microsponges.

Formulation code	Bulk density (gm/ml)	Tap density (gm/ml)	Compensability index (%)	Housnar ratio	Angle of repose
F1	0.38	0.77	50.64	2.02	27^0
F2	0.41	0.49	16.32	1.19	28.35^0
F3	0.44	0.49	10.20	1.11	28.8^0
F4	0.17	0.19	10.52	1.11	29.7^0
F5	0.18	0.21	14.28	1.16	18.45^0
F6	0.17	0.20	15	1.17	28.8^0
F7	0.32	0.49	34.69	1.53	27.45^0
F8	0.34	0.37	8.1	1.08	28.35^0
F9	0.40	0.44	9.09	1.1	27.45^0

Charecterization of Tranexamic acid Microponge

Size analysis of Microsponge

The average particle size of tranexamic acid Microsponges is ranged from 19.4 ± 1.05 to 36.2 ± 1.132. The mean particle size was significantly increases with increasing polymer.

Percentage yield of Microsponges

The percentage yield of tranexamic acid microsponges prepared by Emulsion solvent diffusion method were found to be between 12.83 % to 35.5 %.

Drug Loading Efficiency

The drug loading efficiency of tranexamic acid microsponge by Quasi Emulsion solvent diffusion method ranged from 3.9 % to 8.3%.

Drug content

The percentage of drug content was found to be range from 69.32 to 98.98.

Table 4: Observation for average partical size, percentage yield, % drug loading efficiency and drug content.

Formulation code	Average partical size (µm)	Percentage yield	% drug loading efficiency	Drug content
F1	19.4±1.05	12.83	8.0	91.12
F2	21.7±1.02	35.5	7.08	92.67
F3	24.8±1.04	29.86	3.9	92
F4	26.5±1.06	25.04	8.3	97.20
F5	29.2±1.09	25.25	8.2	60.97
F6	31.3±1.23	23.75	8.1	97.41
F7	34.1±1.18	32.83	4.45	69.32
F8	35.6±1.34	30.3	4.45	96.32
F9	36.2±1.32	32.46	4.5	98.98

In vitro Drug Release

Table 5: Observation for In Vitro Drug Release Dada of Formulation F1-F9.

Times	F1	F2	F3	F4	F5	F6	F7	F8	F9
5 m	12.37	13.2	10.97	8.16	8.88	11.05	1.8	6.96	22.39
10m	16.53	24	12.99	42.88	18.52	17.85	21	43.63	35.71
15m	24.41	42.21	32.72	48.52	31.47	24.75	30.72	68.46	40.91
20m	26.45	54.86	57.06	50.11	49.71	27.64	48.53	71.60	55.14
30m	36.97	69.22	70.13	75.42	55.92	32.98	61.89	79.92	62.44
45m	45.31	72.82	73.50	78.77	74.58	45.26	72.90	83.67	65.42
60m	49.60	88.10	76.11	84.30	79.47	57.87	76.42	84.21	71.34
90m	60.74	94.66	79.18	86.16	81.26	62.84	79.17	86.64	75.86
120m	72.26	98.24	86.02	87.87	83.31	74.58	81.67	89.41	78.74

DISCUSION

The melting point of tranexamic acid was pragmatic in range of 384-390°C (literature standard 386-392°C). As experimental values were in good agreement with standard, procured drug was supposed to be pure. By determining the organoleptic properties, it was observed the drug was found to be white color, and odorless. Solubility study showed that tranexamic acid is freely soluble in water and glacial acetic acid, very slightly soluble in alcohol. Tranexamic acid microsponge of particle with fairy white tincture were obtained by quasi emulsion solvent diffusion technique. With good flow properties than as compared with Pure drug. The Percentage yield of tranexamic acid microsponge prepared by quasi emulsion solvent diffusion method were found to be between 12.83 % to 35.5%. The drug loading efficiency of microsponge by quasi emulsion solvent diffusion method ranged from 3.9% to 8.3%. The average partical size of tranexamic acid microsponges found in between range from 19.4 ± 1.05 to 36.2 ± 1.132. The percentage of drug content was found to be range from 69.32 to 98.98.

CONCLUSION

It can be concluded that the results obtained in study that the quasi-emulsion solvent diffusion technique is an most effective technique to formulate the microsponges based delivery system of the tranexamic acid with maximum production yield and drug loading efficiency. Tranexamic acid microsponges prepared with polymer eudragit S 100. The present study, has satisfactory attempt to prepared the formulate and evaluate of tranexamic acid laded microsponge with compatibility with other components. Formulation having biocompatible polymer such as eudragit S 100 are used to the preparation. In this system are entrapment of its ingredient are contributes toward improve stability, enhanced formulation flexibility and reduced side effects.

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