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COMPARATIVE EVALUATION OF PHARMACOKINETIC PROFILE OF HERBAL AND SYNTHETIC POLYMER BASED DELIVERY SYSTEM

BHARDWAJ H[1*], GUPTA A[2], JANGDE RK[1] AND KHUNTE S[1]

1: University Institute of Pharmacy, Pt. Ravishankar Shukla University Raipur, Chhattisgarh (492010) India

2: Shri Rawatpura Sarkar Institute of Pharmacy Kumhari, Durg (C.G) (490042) India

***Corresponding Author: Dr. Rajendra Jangde; E Mail: rjangdepy@gmail.com**

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ABSTRACT

The formulation and evaluation of herbal and synthetic polymer-based microspheres for a targeted drug delivery, herbal polymer arrowroot is effectiveness, biodegradable, polysaccharide, and natural polymers chitosan is used in preparation and comparison as a (standard natural polymer) polymer-based microspheres and establishment of arrowroot microspheres. Several drugs delivery system for targeting the organ and tissue, the drug release provides a therapeutic effect of drugs and desired concentration in the body. Naturally polymers-based microspheres are used as a carrier system for a targeted tissue, organs and used to effective manner. These are consisting of protein, natural and synthetic which are biodegradable floras, particle size having less than 200 µm. It is prepared by solvent evaporation methods and cross-linking methods. Arrowroot-based ethyl cellulose microsphere is prepared by solvent evaporation technique using ethyl cellulose and poly vinyl alcohol (stabilizer). The prepared microspheres are tested for particle size, percentage entrapment efficacy, zeta potential, and in vitro drug release. Controlled /sustained drug delivery system provides, minimize the side effect of conventional drug delivery, and increase the therapeutic efficacy of drug. The various applications of this microsphere, such as cancer cell and colon targeted drug delivery system, are critical for the safe and effective in-vivo drug delivery. The goals of this study are to highlight some key aspects of herbal

microspheres as a novel drug delivery system. It was determined that the developed herbal microspheres formulation is a significant, therapeutically effective, and cost-effective vehicle for drug delivery.

Keywords: Arrowroot Polymer, Chitosan, ethyl cellulose, Solvent evaporation, Microsphere's drug delivery system

INTRODUCTION

Herbal microspheres are prepared to overcome drug problems, minimize side effects, and be cost effective. It boosts therapeutic efficacy and targets specific tissues in the body. Arrowroot and chitosan are polymers found in plants and animals that deliver a therapeutic active constituent, bind specific cells, and regulate medication release. Drug delivery based on natural and synthetic polymers, used in the context of chronic disease. Arrowroot and chitosan have piqued the interest of biomedical and pharmaceutical researchers. Polymers are biodegradable, have low side effects, and are biocompatible in nature. Herbal microsphere formulations are used as oral, parenteral, and targeted drug delivery systems. Chitosan microspheres are followed by passive diffusion after being physically and chemically metabolized in the body.They are also the practical problem challenges associated with the applications of microspheres, such as the high toxicity of anti-tumor drug itself and the high burst release of general microspheres anti-tumor small molecule drug have not been developed as suitable long-acting microspheres preparation for clinical application, the use of herbal medicines has gained world-wide attention due to many patients' compliance and therapeutic efficacy **[1]**. The knowledge of such plants and their use by indigenous cultures is beneficial to the conservation of traditional systems of medicine biodiversity and the promotion of health care systems. In the future, combining different strategies for microsphere preparation will play an important role in novel drug delivery **[2, 3]**. The targeted drug delivery system is designed to try to concentrate drugs in microspheres **[4]**. A microsphere is a small spherical micro particle with a diameter ranging from 1m to 1000 nm **[5]**. The microspheres are free-flowing particles made of natural or synthetic polymers that are biodegradable. Because the medicine is targeted at a specific spot, it has no effect on the immediate muscle **[6]**. So, if changed, it is the dependable means of delivering the medicine to the target location with specificity and maintaining desired concentration at the concentration site without undesired side effects. They establish a lot of thought not just for long-term release, but also for anticancer

treatment targeting for malignant cells. Microspheres will play a role in innovative medication delivery soon, namely in diseased cell targeting **[7]**, diagnostics, genes and genetic material, safe targeted and effective distribution, and augmentation as a miniature version of infected organ and skin in the shape. There are currently 13 microsphere products on the market, but only three of them are loaded with small molecules, and two of them are recognized to be anti-cancer medications **[8]**. They were also the applicable problem difficulties related to micro particle techniques. Dosage form of arrowroot prepared in precise amounts to provide specific nutritional and cosmetic benefits, as well as diagnosis and cure disease in humans and mammals **[9]**. Whole plant extraction percolation distillation purification, attentiveness, or fermentation is examples of herbal preparations **[10]**. Chitosan also has high bio adhesive properties and can slow the rate of medication clearance from the location, hence improving the bioavailability of pharmaceuticals fused **[11]**. Arrowroot-loaded microspheres are used to administer controlled/sustained release of a variety of medications, as well as to increase the bioavailability of degradable substances like protein and the absorption of hydrophilic substances across cell tissue. These microspheres are being tested for both parenteral and oral drug delivery. Herbal medications are used to support the health-care system, and herbal medicine has a wide range of therapeutic effects **[12]**. Such plants, as well as their active constituents, have been extensively used in the conversion of traditional medical systems **[13]**.

MATERIAL AND METHODS

Arrowroot powder obtained from goal market Raipur and chitosan obtained from gift sample of Chemichito natural product, Chennai, India, ethyl cellulose, poly viny alcohol and chloroform, TPP, obtained from college laboratories.

Preparation of Microspheres by using Solvent Evaporation Technique

Weighing 1.5g of ethyl cellulose as a solid phase and 20 ml of chloroform as a solvent to form an equal polymeric solution than added herbal polymers, which were previously weighed 1.5g of arrowroot polymers thoroughly mixed in chloroform solvent. In thechloroform solvent mixture, 100ml of aqua solution (distilled water) and 200mg poly vinyl alcohol were added. This compound was stirred at room temperature for 3 hours at 500 RPM (Remi motor). After the chloroform was completely removed from the stirrer using the evaporation method, round shape microspheres were produced. The microspheres were filtered and dried at room temperature for 24 hours **[14]**.

Table 1: Formulations of arrowroot containing microspheres

Formulations	Polymers(gm)	Arrowroot (mg)	Ethyl cellulose (mg)	Chloroform (ml)	PVA (mg)
F1	1.5	150	-	250	200
F2	1.5	200	-	250	200
F3	1.5	250	-	250	200
F4	1.5	300	-	250	200
F5	1.5	-	150	250	200
56	1.5	-	200	250	200
F7	1.5	-	250	250	200
F8	1.5	-	300	250	200
F9	1.5	-	350	250	200

Cross Linking methods

A solution of Chitosan was prepared by adding the specified quantity of drug to lactic acid solution (2.4% v/v) followed by stirring for one hour. Separately, chitosan stayed evaporated in absolute solvent ethanol and this mixture have been added to the previously prepared drug solution and stirred for 15min. This resulted in the formation of chitosan dispersion in drug solution. The ratio of drug solution to that of chitosan was 1:5. 20 ml of sodium tripolyphosphate (TPP) solution was placed in a beaker and 10 ml of the TPP dispersion in solvent **[15]**.

Table 2: Formulation of chitosan containing microspheres

Formulation No.	Conc. Of chitosan polymers (%w/v)	Conc. of drug (% w/v)	Cross linker (TPP) (% w/v)	Curing time (hrs.)	Volume of drug solution (ml)
F1	1.5	0	6	2	50
F2	2.0	0	6	2	50
F3	2.5	0	6	2	50
F4	1.5	0	6	2	50
F5	2.0	0	6	2	50
F6	2.5	0	6	2	50
F7	1.5	0	6	2	50
F8	2.0	0	6	2	50
F9	2.5	0	6	2	50

Evaluations of microspheres

Determination of particle size

Determination the particle size of arrowroot microsphere using the optical microscopic method. Around 100 particles of microspheres were considered for particle size analysis by mean of a standardized optical microscope **[16]**.

Morphological Study using by Scanning Electron Microscopy

Arrowroot based microspheres were scanned and examined under scanning electron microscopy HITACHI SU 1500, Japan, connected with fine coat of JEOL JFC- 1100E ion sputter **[17]**. The microspheres containing samples was loaded on copper sample holder which is coated with carbon tailed.

Swelling index

Swelling index of prepared microspheres were determined by using the formula of Swelling index = (Mass of microspheres-mass of dried microspheres) x100 **[18]**.

Drug percentage entrapment efficiency

Prepared microspheres corresponding to 50mg of polymers were taken for estimation. The herbal microspheres crushing and separate the coting part of 0.1N HCL (pH-1.2) coated were transferred to 100 ml of volumetric flask and volume was made up using 0.1 N HCL (Ph-1.2). The drug solutions were removed, and percentage drug entrapment were measured after addition of suitable dilutions spectrophotometrically (Ultraviolet V 1700, Shimadzu Japan) at212 nm **[19]**. The amount of drug polymersloaded and entrapped efficiency in the microsphere was calculated by the following methods.

$$\% \text{ Drug loading} = \frac{\text{Weight of the drug loaded in the microspheres} \times 100}{\text{Total weight of the microspheres}}$$

$$\% \text{ Drug Entrapment} = \frac{\text{Amount of drug present (DC)} \times 100}{\text{Theoretical drug loaded expected}}$$

$$\% \text{ Yield} = \frac{\text{Practical yield} \times 100}{\text{Theoretical yield}}$$

Surface charge (Zeta- Potential)

Prepared microsphere wasrecognized with Zeta Nano ZS, Malvern instruments. The quantities were carried out of KCl 0.1N aqueous solution. The determinations of prepared microspheres were diluted with KCl solutions. Suitable value was adjusted and typical for temperature in 20 °C **[20]**.

Differential Scanning calorimetry

DSC analysis was used to characterize the deviation, melting point, polymorphism, if any experimental during the research on the microspheres. Differential scanning calorimetry of arrowroot microspheres as a test sample and chitosan microspheres is standard natural microspheres. Carried out by using a DSC 204 PHOENIX NETZSCH system over the temperature range 30ºC to 300ºC at a scanning rate of 10 ºC /minute **[21]**.

FTIR spectroscopic Analysis

Fourier transform infrared spectroscopic studies of arrowroot and chitosan microspheres, were done by recording the

corresponding FT-IR Spectra in the Bruker IFS66v INDIA over wave number range of 400-4000 cm-1 The major peaks which are present in pure drug Arrowroot Powder are also present in the physical mixture **[22]**.

Stability studies

Stability studies of drug have been definite as the preparation in specific bottle to remain within its chemical, physical, toxicological, and therapeutic condition. Stability studies of drug to give evidence on how much quantity of drug distress with time under the environmental influence such as light, temperature, moisture, and optional storage environments. ICH rule of study and storage environments accelerated testing -40 °C/75 relative humidity for 6 months, the accelerated stability stud of the drug preparation was taking as per the ICH guideline **[23]**.

RESULTS AND DISCUSSION

Preliminary study data

Drug excipients compatibility studies by physical observation

Arrowroot and chitosan microspheres were diverse with numerous proportions ofexcipients exposed no color alteration at the termination of three months and that is showing no drug-excipients interaction **(Table 3)**.

Infra-red Spectroscopy

Arrowroot microspheres infra-red spectra were found to be natural standard chitosan microsphere, specific polymers are shown in **Figure 1 and Figure 2** arrowroot and chitosan polymers are present in polymer spectrum.

Particle size and Shape studies

Prepared microscope is resolute by optical microscope by using the ocular micrometer and stage micrometer show in **Table 4 and Figure 3, 4 and 5** preparation F1 to F4 covering arrowroot and chitosan microspheres, average particle size control was observed in range from 278±7.14 µm to 107.2 ±9.97µm. and design F4 to F9 having arrowroot and chitosan average particle size was found to be in rages from 557 ±12.51 µm to 391 ± 10 µm.

Table 3: Data of some physiochemical studies

Parameter	Polymers	Result	Reported
Melting point	Arrowroot Chitosan	113±3ºC 109±5 ºC	118ºC 139ºC
pH	Arrowroot Chitosan	5.7± 1 6.2 ±2	4-6 6.5
Solubility	Arrowroot Chitosan	Soluble in ethanol, glycerol, ether and benzene, petroleum ether, chloroform etc.	Soluble in hexane, ethanol, insoluble in ether, chloroform benzene oils and fat, petroleum ether.

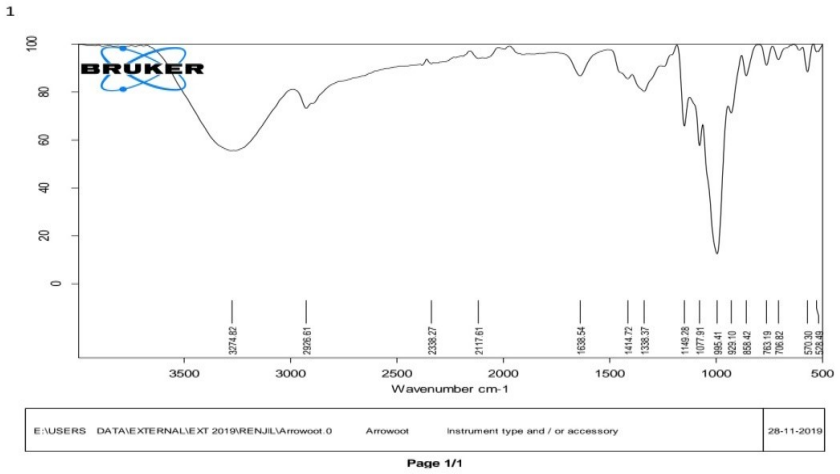

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Figure 1: FT-IR study of Arrowroot microspheres

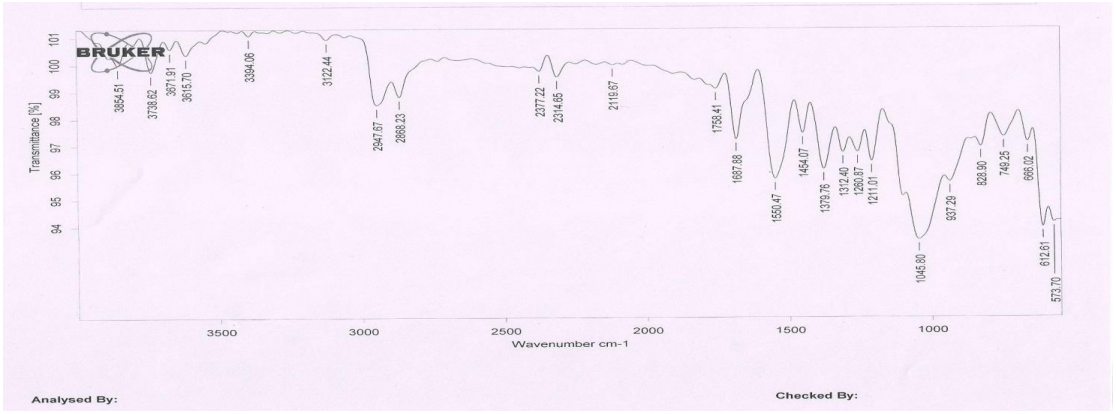

Figure 2: FT-IR study of Chitosan microspheres

Table 4: Particle size of Arrowroot and Chitosan Microspheres

Formulations	Average particle size of arrowroot microsphere (µm)±SD	Average particle size of chitosan microspheres (µm)±SEM
F1	93±6.35	47.6±2.73
F2	90±11.28	76±6.53
F3	56±12.42	99.8±8.62
F4	278±7.14	107.2±9.97
F5	991±10.73	113.1±7.17
F6	743±12.24	150.3±5.32
F7	617 ± 7.87	272±12.51
F8	589 ±10.34	390±11.46
F9	557 ±12.51	391±10.73

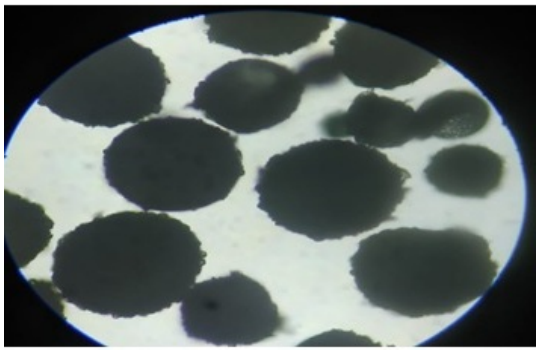

Figure 3: Microscopy of arrowroot microspheres

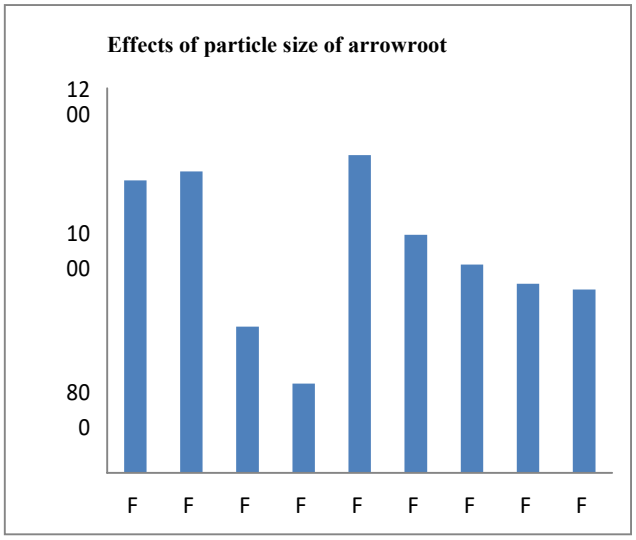

Figure 4: Effect of particle size of arrowroot

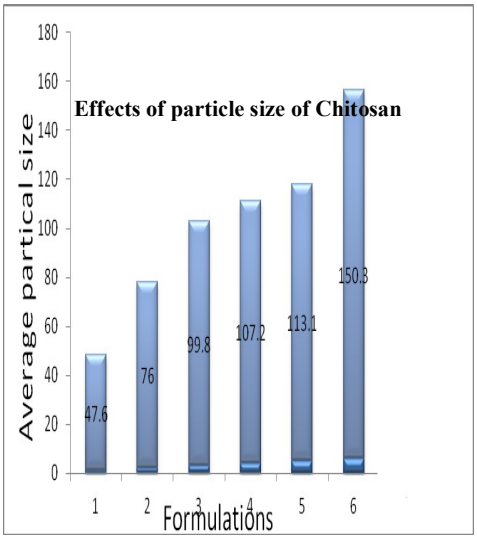

Figure 5: Effect of particle size of chitosan

Scanning electron microscopy

The assurance of structure and surface geomorphology was finished by checking electron magnifying lens HITACHI SU 1500, Japan. SEM examination of the examples uncovered that all microspheres arranged were circle molded fit. The microspheres of Arrowroot microspheres and chitosan were smooth, round and somewhat accumulated particles when contrasted and the microspheres of chitosan which were permeable, harsh, terribly, discrete circular. Examining electron photomicrographs of the Arrowroot details A, B, C and D and Chitosan P, Q and R are displayed in **Figure 6 and 7**.

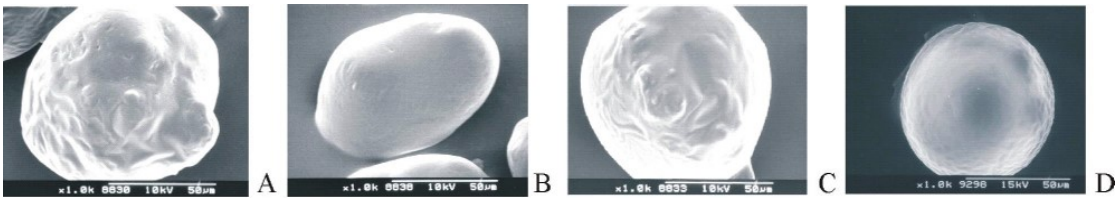

Figure 6: SEM images of Arrowroot A, B and C, D

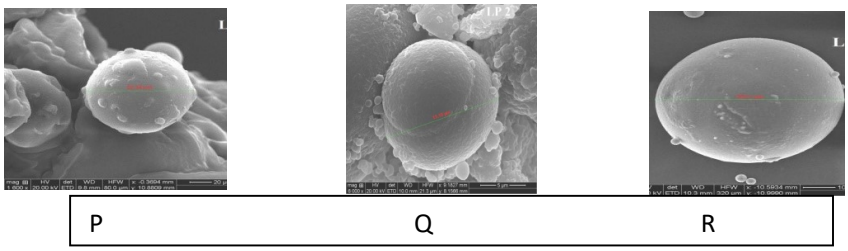

Figure 7: SEM image of Chitosan microsphere P, Q, R

Percentage yield

Rate yield of various detailing F1 to F9 were determined and the yield was viewed as, 75.73%, 67.68%, 61.54%, 81.13%, 71.4%, 70.70%, 59.68% and 55.50% individually. The rate pragmatic yield marginally diminished as the polymer proportion expanded. The consequences of all definitions F1 to F9 of microsphere are displayed in **Table 5 and Figure 8 and 9**.

Surface charge (Zeta-potential)

The surface charge was identified by using Malvern Instrument Zetasizer. The estimations were done of KCl 0.1N aquas arrangement. Preceding the assurance's microspheres was weakened with KCl arrangement. The deliberate qualities were adjusted to a standard reference for temperature of 20°. The outcomes are the method for three-fold tests Properties of Miniature Molecule **(Table 6)**.

DSC Analysis for formulations

Warm properties of the unadulterated medication and the actual combination of medication and excipients were breaking down by Various Checking Calorimeter 60. The examples were warmed in a specifically fixed aluminum skillet. Temperature runs for each example test were set from 30 to 300ºC at a warming pace of 100C/min, utilizing nitrogen as cover gas. Differential scanning calorimetry was used to examine the melting and crystallization behavior of materials. DSC thermo gram of pure Arrowroot powder shows sharp endothermic peak 113.3ºC. DSC thermogram are shown in **Figure 9**.

Table 5: Practical Yield of Arrowroot and Chitosan Microspheres

Formulations	Theoretical Wt. (mg)	Practical Yield (mg)	%Yield (Arrowroot)	% Yield (Chitosan)
F1	1000	748	75.32	76.4 ± 2.72
F2	1500	1095	75.73	74.4 ± 1.39
F3	2000	1296	67.68	72.84 ± 0.84
F4	1000	764	61.54	78.33 ± 0.93
F5	1500	1097	81.13	80.64 ± 1.12
F6	2000	1288	71.4	82.68 ±2.1
F7	1000	747	70.7	84.45 ±6
F8	1500	1089	59.68	86.23 ±3.5
F9	2000	1310	55.50	88.59 ±7.1

Figure 8: Arrowroot microsphere

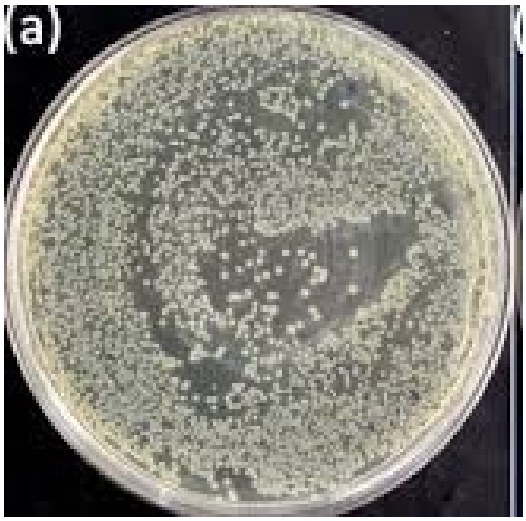

Figure 9: Chitosan microspheres

Table 6: Zeta-potential Arrowroot and Chitosan Microspheres

Formulations	Particle size (um+Sd)	Zeta potential Arrowroot (Mv+Sd)	Zeta potential Chitosan (Mv+Sd)
F1	913±6.35	8.64 ±0.57	15.3±0.52
F2	940±11.28	13.43 ±	17.43 ±
F3	456±12.42	0.21	0.35
F4	278±7.14	14.91 ±	24.1 ±
F5	991±10.73	0.81	29.4

Table 7: DSC melting point of selected Polymers	
Polymers	DSC melting point in ºC
Arrowroot	113.3 ºC
Chitosan	149.7 ºC

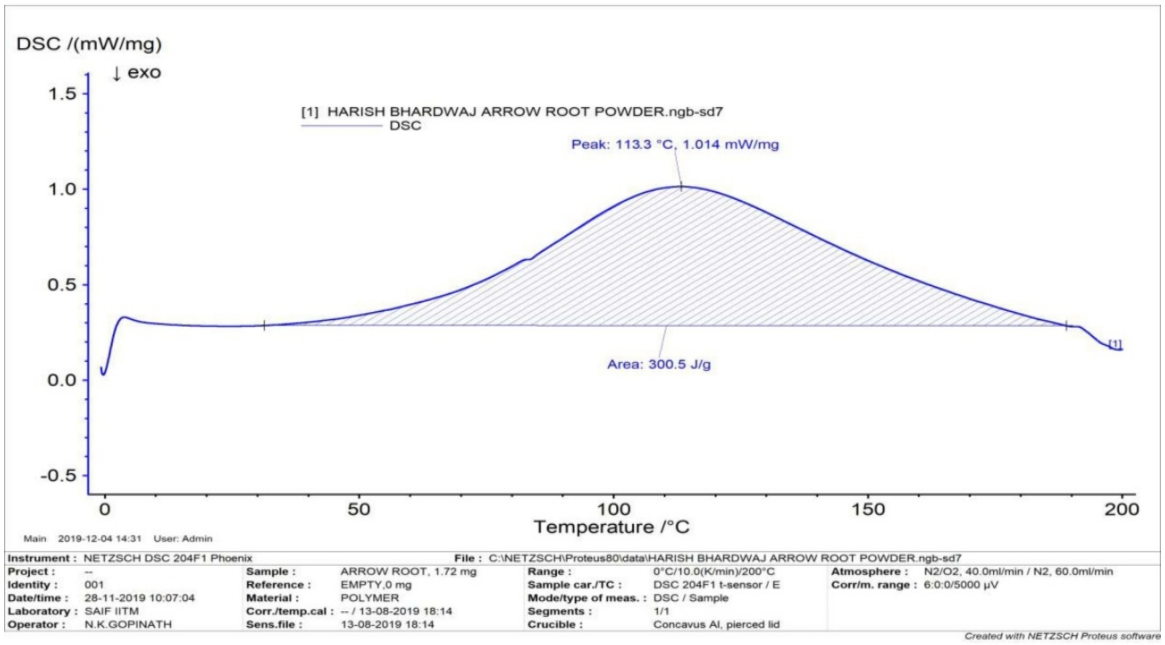

Figure 10: DSC Curve of Arrowroot Microsphere

CONCLUSION

The current review describes an innovative effort to define chitosan and arrowroot microspheres using natural polymers such as arrowroot and chitosan, as well as manmade polymers such as Ethyl cellulose. A dissolvable solvent evaporation technique was used to make arrowroot microspheres. Furthermore, chitosan was prepared using a cross-linking process, and several assessment boundaries were examined. Based on the results, the following inferences could be drawn: FTIR analysis revealed that the polymers are viable with all excipients. The molecule size of the pre-arranged microspheres was also within the range of 936.35 to 55712.51m, while chitosan microspheres were permeable, unpleasant, horribly, discrete round particles. SEM examination of the microspheres shown that arrowroot and chitosan encompassing microspheres were plane, circular, and marginally collected particles when compared to chitosan microspheres, which were permeable, unpleasant, horribly, discrete. As a result, detailed microspheres appear to be a promising candidate for use as an oral controlled medication conveyance framework in extending medication maintenance in the GIT.The goals of this study are to highlight some key aspects of herbal microspheres as a novel drug delivery system. This review will cover the definitions, concepts, types, evaluation, and characteristics of microspheres, as well as

the various methods and techniques used to prepare them. It was determined that the developed herbal microspheres formulation is a significant, therapeutically effective, and cost-effective vehicle for drug delivery.

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