Research Article

FORMULATION AND *IN-VITRO* CHARACTERIZATION OF LAMIVUDINE EMBEDDED NATURAL RESIN MICROSPHERES USING OLIBANUM AS DRUG CARRIERS

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ARTICLE INFO

Article history:
Received 29 May 2020
Revised 09 June 2020
Accepted 15 June 2020

Keywords:
Controlled release, Lamivudine, Microspheres, Olibanum, Resin

ABSTRACT

The present study was aimed to formulate and characterize controlled release microspheres of lamivudine using a natural resin olibanum as novel microencapsulating carrier. An o/o emulsification-solvent evaporation method was employed for design of different batches which can be made industrially feasible. The batches designed were characterized in-vitro for formulation yield, encapsulating efficiency, particle morphology, flow properties, infrared spectroscopy (FTIR), X-ray diffraction (XRD), differential scanning calorimetry (DSC), release behavior, release kinetics etc. The drug loaded resin microspheres were resulted to be discrete, free flowing and roughly sphere-shaped. Microencapsulation efficiency revealed in narrow and even distribution of lamivudine among various formulated batches. XRD and DSC reports resulted a minor change in lamivudine physical state. Release of lamivudine from optimized batches was slow with release period of over 24 hours. Release was found to be dependent on ratio of core to coat in the formulations. The mechanism drug release was detected to be following Fick's law. Various processing parameters like as core to coat ratio, stirring speed, concentration of surfactant, processing medium volume, etc. for the process of emulsification was identified in relation with the microencapsulation efficiency and release behaviors of drug. The drug loaded resin microspheres revealed release characteristics in a controlled manner and established to be ideal for once a day dosing.

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INTRODUCTION

Drug discovery itself isn't sufficient in treating diseases; apart from this accurate dosing and targetingthe drug are also equally essential for the clinical success. Researchers involved in the design ofsustained or controlled release dosage forms particularly focus in to these areas to increase the effectiveness of drugs for specific dosage regimens[1]. Controlled release dosage regimens are especially designed at controlling the discharging of the drug at a therapeutically rate of effectiveness, prolonging therapeutic response by delaying the duration of drug delivery and targeting the drug to a specific tissue[2].

Among the various orally administered controlled release dosage forms, microparticles(microspheres and microcapsules), produced by microencapsulation process are gaining a lot of popularity[3]. Furthermore these are being multiunit systems that expanded over a significant surface area of gastrointestinal mucosa and avoid exposure to a locallyelevated concentration of drug, when accessedin comparison with differentmono unit dosage regimens on persistent dosing. Apart from the vagaries of gastric emptying and dissimilar motility rates the gastrointestinal tract, these release the drug uniformly [4, 5]. Several standard text books had explained microencapsulationprocess by different polymerswith applications.[6-8].

Though several types of polymers are there to provide as a release controlling microencapsulating agent but employing natural biodegradable polymeric materials to extend the releaseof drugs is constantly an area of effective research instead the arrival of various biodegradable polymers from synthetic sources. Because of abundant availability in the nature, economical, living organism's products, readily biodegradable, non-toxic characteristics and capability to undergo chemical modifications,natural polymers remains eye-catching primarily [9].In thecurrent investigationolibanum resin was utilized as a natural release retarding microencapsulating agent. It is an oleo gum resin procured from the incised trunk of *Boswelliaserrata*tree(family:Burseraceae). It is generally known as Indian Olibanum, Sallakiguggul, and Salai gum.Geographically they belong to tropical regions of Asia and Africa.Olibanum composed of generally 56-60% of an acid resin, 30-36% of gum and 3- 8% of volatile oil. Gum generally contains arabinose with littlequantity of galactoseand xylose [10, 11].Resins are generally high molecular weight substances [12]. Approximate molecular weight and degradation pathway

of olibanum resin isn't known clearly. The molecular weight of its major constituent (i.e., Boswellic acid) is found to be 456.711 g/mol [13]. It is found to be safe and well tolerated while taken orally [14].

Solvent evaporation technique is a most suitable method for the preparation ofmicroparticles. Here the drug is solubilized or dispersed within an organic polymeric solution, which is subsequently emulsified in a continuous oil or aqueous phase. After removing the solvent, the microparticles are formed [15].

Acquired immune deficiency syndrome (AIDS), resulting in life-threatening opportunistic infections and malignancies is caused by Human Immunodeficiency Virus (HIV), is an immuno suppressive disease [16]. Since its first inception in California about three decades ago in 1981, more than 25 million populationsthroughout the world have been eradicated by this dreaded killer, [17]. A report by UNAIDS 2012, on global AIDS epidemic revealed,worldwide approximately34 million populations were living along with AIDS at the end of 2011 and approximately 1.7 million populationkilled due to thereasons related with AIDS in 2011[18]. Around 30 different types of antiretroviral products, fabricated till now either alone or in combination for treatment of HIVpatients [19]. But the major drawbacks of antiretroviral with the long-term therapy, and their high cost [20, 21].

The (-)-enantiomer of 2′,3′-dideoxy-3′-thiacytidine or lamivudine, is a synthetic nucleoside analog whichhinders HIV reverse transcriptase and is being increasingly used as a powerful antiretroviral agent for treatment of AIDS[22]. Lamivudine, chemically $C_8H_{11}N_3O_3S$ is soluble in water with a molecular weight of 229.256 g/mol.Because of its rapid absorption, itproduces a bioavailability of around 82% following oral intake. Conventional oral dosage forms of lamivudine are administered several times a day (150 mg bid), because of its moderate half-life (5-7 hours),[23, 24]. However these conventional oral dosage formsare associated withseveral limitations, like adverse side effects producing from drug buildup duringmultidose therapy, high cost of therapy, poor patient adherence,etc. Therefore the inception of controlled release of lamivudine would be advantageous in contrast with the conventional dosage regimens [25]. In the present study, anti retroviral drug lamivudine loaded microspheres were developed by using natural, biodegradable, non-toxic olibanum resin for controlled release.

MATERIALS AND METHODS

Lamivudine and resin olibanum wereprocured as gift samples from HETERO DRUGS Ltd. (Hyderabad, India) and Girijjan Corporation, (Viasakhapatnam, India) respectively. Diethyl ether (Qualigens), acetone (Merck), span 80 (Finnar chemicals), light liquid paraffin (Qualigens), etc are employed.Various reagents used are of pharmaceutical grade and areused as obtained.

Processing of microspheres

Acetone was used as the polymer solvent for preparation of lamivudine-loaded microspheres by an industrially possible emulsification solvent evaporation method.Span 80was used as emulsifying agent along with light liquid paraffin as preparatory medium.The n-hexane was used as washing liquid for themicrospheres. For preparation of microspheres with different drug and polymer ratios (w/w), required quantity of lamivudine was accurately weighed and solubilized in a polymeric solution (w/v) of olibanum resin in acetone.In all cases, the drug and solvent quantities are kept uniform with a change ofratio of polymer to drug.The harvesting medium was produced by dispersing the emulsifying agent span 80 in liquid paraffin. The organic phase containing drug was added into the harvesting mediumkept under continuousstirring rate of 1000 rpm to emulsify the poured dispersion in to fine droplets contained in a 500 ml beaker by using a mechanical stirrer having digital speedometer display (Model RQT 124). Stirring was continued for approximately 3 hrs at room temperature during which acetone was completely evaporated. The microspheres were collected after decanting the light mineral oiland washed three times at room temperature to separate the traces of paraffin oil with 100 ml of n-hexane.Laterto obtain discrete microspheresthe filter cake wasdried with air for 12 hrs after separating by vacuum filtration [26].

Characterization of microspheres

Lamivudine Estimation

Correctly100 mg of drug containing microsphereswere weighed,crushed and dispersed in specific volume of 7.4 pH phosphate buffer. The whole content was blended at 1000 rpm for around 2 hrs. Subsequently the resulting solution was filtered and diluted properlybefore analyzingby a UV-visible spectrophotometer forestimation of drug at 270.01 nm using[27].

Process yield (%) and microencapsulation efficiency (%)

The ratio of weight of the dried microspheres to that of theoretical amount at room temperature is known as yield, generally represented as percentage. Process

yield or % yield [28] and microencapsulation efficiency[29] weredetermined by utilizing the equations given below.

$$\text{Process yield (\%)} = \frac{\text{Weight of microspheres procured}}{\text{Total raw material weight}} \times 100$$

$$\text{Microencapsulation efficiency (\%)} = \frac{\text{Practical drug content}}{\text{Theoritical drug present}} \times 100$$

Micromeritic properties

Various micromeritic properties, likebulk density, tapped density and angle of reposewere calculated. All the experiments were performed in triplicate. The angle of repose was estimated using static funnel method[30].

Size distribution of particles by sieve analysis method

A mechanical sieve shaker with five standard stainless steel sieves (Geologists Syndicate Pvt. Ltd, India) was employed for separation of the microspheres into various size fractions. Themesh sizescontaining of #10, #20, #30, #50 and #80 were arranged in adecreasing order of their openingsize. Accuratelyweighed quantity of microspheres waskept on the topmost sieve. For around 10 minutes, the sieves were shaken, and the particlesremain on everysieve were estimated [31]. The experiment was carried out in triplicate.

FT-IR studies

The interactions betweendrug and polymer were studied by using FT-IR spectroscopy (Shimadzu, Japan, FTIR-8400S). Both for pure drug lamivudine and microspheres the spectra were recorded. KBr discs method was followed. The range of scanning was within 400–4000 cm^{-1} and having 4 cm^{-1} resolution [32].

Scanning electron microscopy (SEM)

A scanning electron microscope (LEO 440i, England) was utilized to study themorphological characteristics of the microspheres. Before analyzing after mounting on an aluminum sample stub with adhesive tape, a low humidity chamber was used to keep the samples for 12 hrs.Prior to this a high vacuum evaporator was used to coat the samples with gold-palladium under an argon atmosphere for 60 sec.Images of microspheres were taken at an acceleration voltage of 20 kV[32].

Differential scanning calorimetry

Differential scanning calorimeter (DSC 60, Shimadzu, Japan) was used to study the thermal behavior of the drug as well as microspheres. Around 5 mg samples were placed in 50 μm perforated aluminum pans and sealed thereafter. Over a temperature range of 5–300^0 C in nitrogen atmosphere the samples were heated with a rate of 10˚/min[1].

X-ray diffraction analysis

Philips PW 170 system (Philips USA) with Cu-Kα radiation (400 kV, 30 mA, and scan speed 1˚/min) was utilized for X-ray diffraction analysis of drug as well as microspheres in order to check the solid state of lamivudinepresent insidethe microspheres[32].

Determination of *In-vitro lamivudine release*

A paddle type dissolution apparatus (USP-XXIII, ETC-11L, Electrolab, Mumbai) was used to determine the *in-vitro* release rate of lamivudine from different batches ofmicrospheres.The experimentation were designed for 24 hours containing 900 ml of dissolution medium (phosphate buffer pH 7.4) maintained at 37±0.5^{0}C.The rotational speed of stirrer was maintained throughout at 100 rpm [33].Microspheres containing around 100 mg of drug was accurately weighed and placed inside dissolution medium.Sink conditions were ensured during the experimentation. At predetermined time intervals, specific volume (5 ml)of the medium were withdrawnand replenished immediately with equal volume of fresh dissolution medium. The samples were filtered using No.42 Whatman filter paper andassayed spectrophotometrically (Cary 60, Agilent Technologies) at 270.01 nm. The release studies wereperformed three times.

Analysis of the drug release profiles and kinetic models

Several kinetic models like zero-order, first-order, Higuchi etc. were tried out to fit the*in-vitro*drug release profiles of various batches. Respective plot, rate constants were determined from the slope.To find out the diffusion co-efficient (‘*n’*) value,the data generated were fitted withKorsemeyer-Peppas model, which explains the release mechanism of drug.For spherical polymeric devices, when the value of ‘*n’* = 0.43 or less the mechanism of drug release may be Fickian diffusion, when the value of ‘*n’* liesbetween 0.43to0.85,non-Fickian(anomalous) and when ‘*n’* = 0.85 case II transport. When‘*n’*is greater than 0.85, itdenotes super case II transport [34].

RESULTS AND DISCUSSION

Processingof microspheres, process yield (%), quantification of drug andmicroencapsulation efficiency (%)

In the current investigation an effortwas made tocontrol the release rate of lamivudineby designing different batches of resin coatedmicrospheres, with addition of increments of resin to a fixed amount of lamivudine. When an aqueous phase is used asharvesting medium, for encapsulation of hydrophilic drugs, generally they tends to separate out resulting in low microencapsulation efficiency [17].Literature reports revealed thatdepending on the processing conditions, around 80% drugcan leach out to the external aqueous harvesting medium [35]. Therefore in the current studyin order to enhance the encapsulation efficiency an effort was made to encapsulate lamivudineutilizing a non-aqueous mineral oil (liquid paraffin) asharvesting medium with a natural resin such asolibanum.Span 80 having a value of 4.3 on HLB scale was used as an oil miscible non-ionic surfactant to stabilize the process of emulsification by preventing the droplets coalescence and decreasing the interfacial tension.By increasing the drug to polymer ratio (Table 1)an increased process yield was observed. Encapsulation efficiencies were found to be in a constricted range signifying an identical drug distribution withinvarious formulated batches.

Maintaining the drug to polymer ratio steady (LO4), there was statistically a significant ($P < 0.05$, student's t-test) decrease in the encapsulation efficiency of microspheres with varying surfactant concentration (span-80) for the process of emulsification (Table 2). The highest encapsulation efficiency was observed with a surfactant concentration of 1.5%. This may be because the higher surfactant concentration permits the remarkable reduction in the size of the resin-solvent droplets as a result of preventing the droplets coalescence due to reduction in the interfacial tension and, yielding smaller particles with higher surface area, leading the drug leaching out into the processing medium before hardening. Similarly decrease in the surfactant concentration permits the droplets coalescence, resulting in larger particles, with more time to become rigid and greater chances of drug leaching out into the processing medium.When 0.5% span-80 was incorporated, it failed to prevent coalescence of the droplets because of the lower emulsifier content and microspheres were not formed. Therefore it explains that the emulsifier plays a significantjobin the design of microspheres.

The harvesting medium volume also influences the encapsulation

efficiencysignificantly (Table 2). The processing medium volume as changed from 200 to 100 and finally to 500 ml, the efficiency of encapsulation reduced significantly ($P < 0.05$, student's t-test) from 81% to 60% and 57%, in that order. The results may be because of increase in the harvesting medium volume allows the free movement of droplets within the medium, resulting small and uniform microspheres due to decrease in the collision induced aggregation chances. This could also be a reason of the higher rate of drug extraction into the processing medium.Similarly decrease in the volume of processing mediumallows the collision induced aggregation and resulting in larger particles, with more time to become rigid and greater chances of drug leaching out into the processing medium, resulting low encapsulation efficiency.

The change in the stirring speed of the harvesting medium (rpm) also influences the encapsulation efficiencysignificantly of theformed microspheres (Table 2). With a stirring speed of 1000 rpm, highest encapsulation efficiency was observed. Varying the speed from 1000 to 800 and 1200 rpm decrease significantly ($P < 0.05$, student's t-test) the efficiency of entrapment due to the development of bigger and smaller globules respectively, explaining more drug diffusing out of the microspheres prior to their hardening. With a speed of less than 800 rpm, the microspheres use to settle and stick at the bottom of the container forming a solid cake.

Table 1: Data showing core: coat ratio, production yield and microencapsulation efficiency

Formulation codes	Core: Coat ratio	Production yield (%)	Microencapsulation efficiency (%) ± S.D.
LO1	1: 0.25	47.297	75.235 ± 0.59
LO2	1: 0.5	54.239	78.246 ± 1.32
LO3	1: 0.7	56.438	82.697 ± 1.49
LO4	1: 0.8	58.613	81.476 ± 0.72
LO5	1: 0.9	59.769	81.679 ± 0.89
LO6	1: 1	62.531	80.292 ± 1.06

S.D.: Standard deviation; n=3

Table 2: Effect of various processing parameters on microencapsulation efficiency of optimized batch (LO4)

Processing parameters		Theoretical drug content (%)	Experimental drug content (%)	Microencapsulation efficiency (%) ± S.D.
Surfactant concentration (%)	1	55.555	36.981	66.566 ± 1.42
	1.5	55.555	45.264	81.476 ± 0.72
	2	55.555	32.824	59.117 ± 0.91
Volume of processing medium (ml)	100	55.555	33.531	60.356 ± 1.56
	200	55.555	45.264	81.476 ± 0.72
	500	55.555	33.716	57.089 ± 0.79
Stirring speed (rpm)	800	55.555	35.619	64.114 ± 1.23
	1000	55.555	45.264	81.476 ± 0.72
	1200	55.555	33.117	59.611 ± 0.86

S.D.: Standard deviation; n=3

SEM and micromeritic studies

The microspheres were found to be discrete, round, non-cohesive, multinucleate, and uniform in shape (Figure 1) from the SEM photomicrographs studies. It also revealed thatmay be due to the occurrence of drug, the surface of the microspheresfound to be rough,.Various micromeritic studies such as loose bulk density, tapped density, Carr's index, Hausner's ratio, angle of repose, etc. of different formulated batches of microsphereswere evaluated. The results were represented in the table3. The microspheres were found to be non-cohesive as the values of angle of repose, compressibility index and Hausner's ratio areless than 25, 15%and 1.25 respectively for each batch. It confirms that the microspheres don'tneed addition glidant.

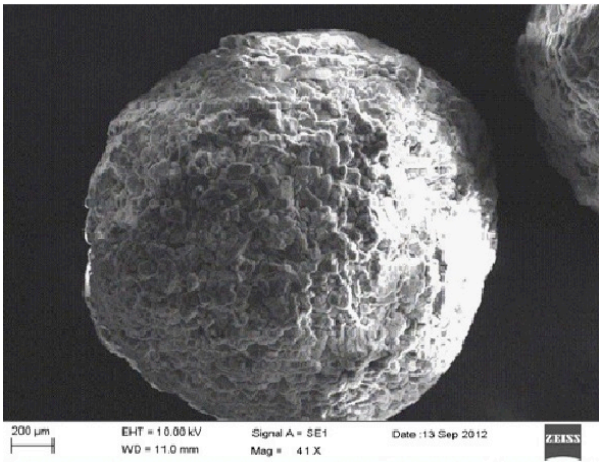

Figure 1: Scanning electron micrographs of lamivudine loaded microspheres (LO4)

Table 3: Flow properties of microspheres

Formulation codes	Angle of repose ± S.D.	Loose bulk density (g/cm^3) ± S.D.	Tapped bulk density (g/cm^3) ± S.D.	Carr's index (%)	Hausner's ratio
LO1	23.73^0±0.561	0.272±0.115	0.301±0.112	10.447	0.905
LO2	24.20^0±0.731	0.263±0.173	0.285±0.173	8.585	0.92
LO3	24.65^0±0.789	0.265±0.057	0.288±0.057	8.655	0.92
LO4	23.18^0±0.762	0.26±0.115	0.277±0.102	6.281	0.94
LO5	22.69^0±0.591	0.265±0.003	0.284±0.072	7.016	0.934
LO6	23.33^0±0.761	0.258±0.057	0.277±0.050	7.408	0.931

S.D.: Standard deviation; n=6

Sieve analysis of microspheres

A narrow particle size distribution was found among various batches of microspheresand the size range was between 450 to 725 μm. The results of sieve analysis also revealed thata large proportion (50-60%) of microspheresin among various batches were within –30 +50 (450 μm) mesh sieves.

FT-IR studies

The absence of any significant interaction between the drug and resin was revealed by the FTIR spectral studies. Absence of any significant degenerative interactions was also found from the spectral peaks.Henceto fabricate the microspheres, the resin could be utilized safely (Figure 2). Lamivudine proved sharp characteristic peaks of carbonyl group at 1650 cm^{-1}(present in the cytidine nucleus).Band peaks at 3319, 3271, and 3197 cm^{-1}remaining to amino and hydroxyl groups.Band Peaks at 1286 and 1161 cm^{-1}remaining to asymmetrical and symmetrical stretching of the C-O-C system (present in the oxathiolane ring). Absence of any modification or interaction between drug and resin were confirmed from the characteristic peaks appeared in the spectrum.

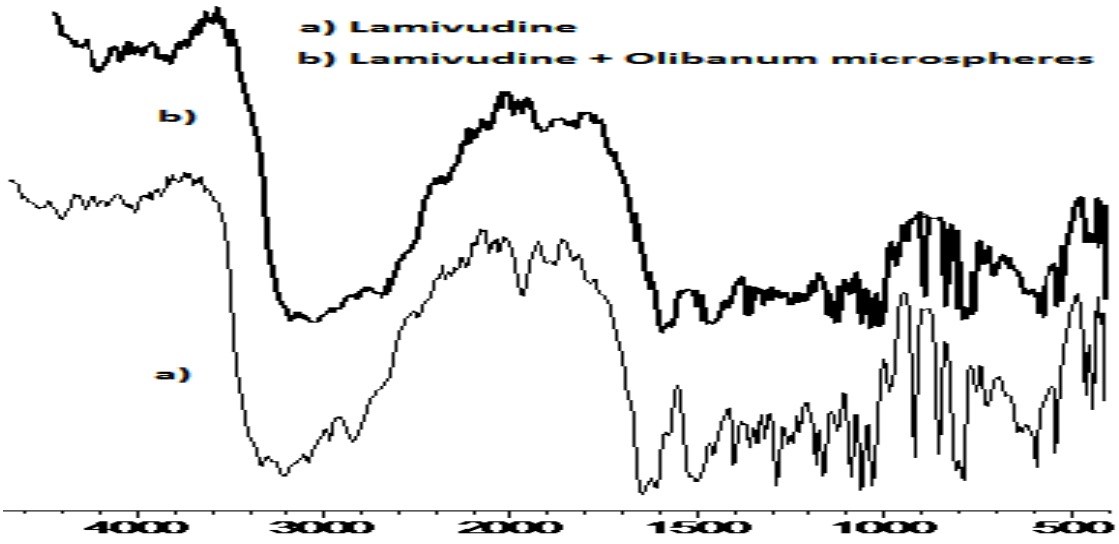

Figure 2: FTIR spectra of pure lamivudine and lamivudine loaded microspheres (LO4)

Differential scanning calorimetry

Through DSC analysis the drug-resin compatibility was confirmed. The thermograms of DSC for pure lamivudine and resin coatedlamivudine microspheresare given in Figure3. From the DSC thermograms it was revealed thatlamivudineshown a pointed endothermal peak coupled with crystal melting pointof 180.82^{0}C, which are similar with the reports for pure drug. In case of the resin coated microspheres analike DSC profile (Figure 4) also obtainedbut with a slight change inthe sharpness of the peak. This confirms aminor reduction in the crystallinity of drug insidemicrospheres. The DSCfinally summarizes that the drugand resinboth are compatible with one anotherwith absence of any drug-resin interactions and drug decomposition withinthe microspheres.

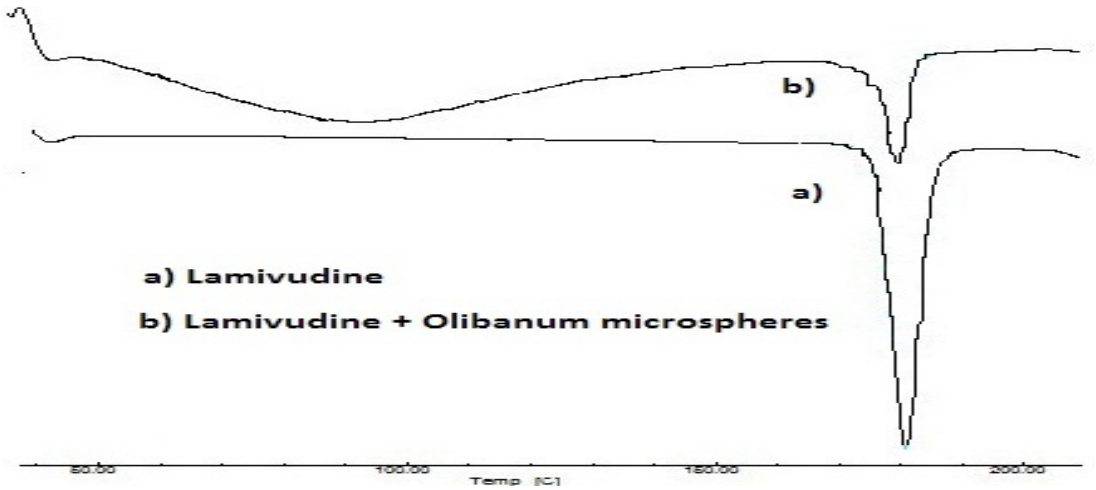

Figure 3: DSC curves of pure lamivudine and lamivudine loaded microspheres (LO4)

X-ray diffraction studies

The diffractogram of pure lamivudine obtained from the X-ray crystallographic data revealed thecrystalline nature of the drug (Figure 4). A similar pattern with a slight reduction in the peak intensity was observed from thediffractogram of resin coatedmicrospheres.This confirms the homogenous dispersion of the drug within the microspheres. The result also explains a minor change in the drug crystalinity within the microspheres. Literature reports on sustained release microspheres had the same interpretation for drugs like zidovudine, famotidine [36, 37].

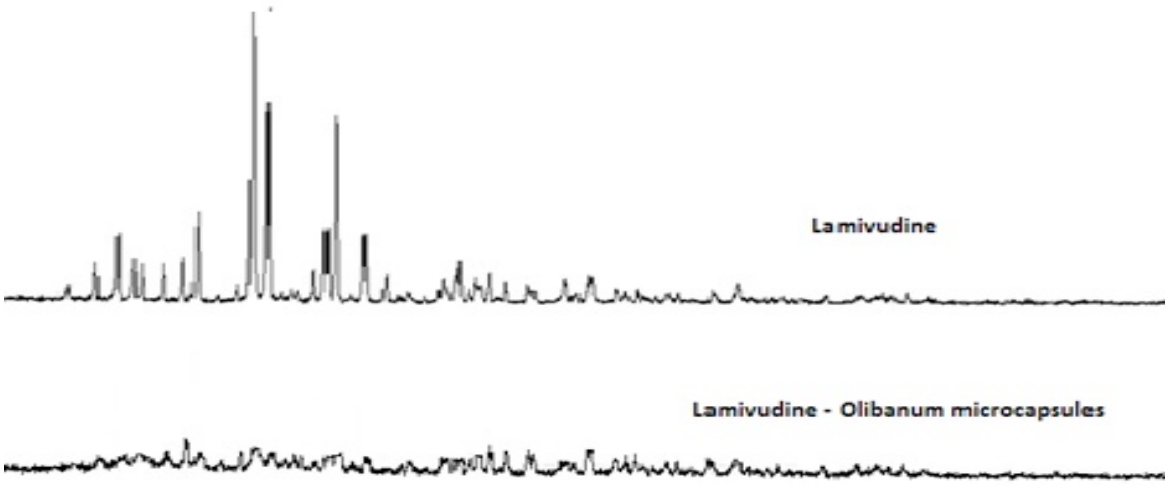

Figure 4: X-ray diffractograms of pure lamivudine and lamivudine loaded microspheres (LO4)

***In-Vitro* drug release behavior**

The *in-vitro* release study was performed in pH 7.4 phosphate buffer dissolution medium fordrugs from various formulated batches. To keep the total surface area of the microspheres constant in order to get comparable results, same size fractions (450 µm) containing equal quantity of drug were selected for the release study from various formulated batches. The release was found to be following a biphasic pattern with an initial ruptureof 31-48% within 1sthr followed by a much slower release. The initial burst may be because of occurrence of drug particles onmicrospheressurfaces and can be ideal to compensate theinitial desired therapeutic plasmadrug concentration required for beginning of pharmacological action.With increase in the resin concentration, drug release rates found to decrease. This may be because higher resin concentrations hasproducedlesser drug concentration gradient between the dissolution medium and microspheres and

increased wall thickness of microspheres[38], resulting a lesser rate of drug release.The release profiles are illustrated in Figure 5. The best controlled release *in-vitro*was scrutinized for LO4 batch.

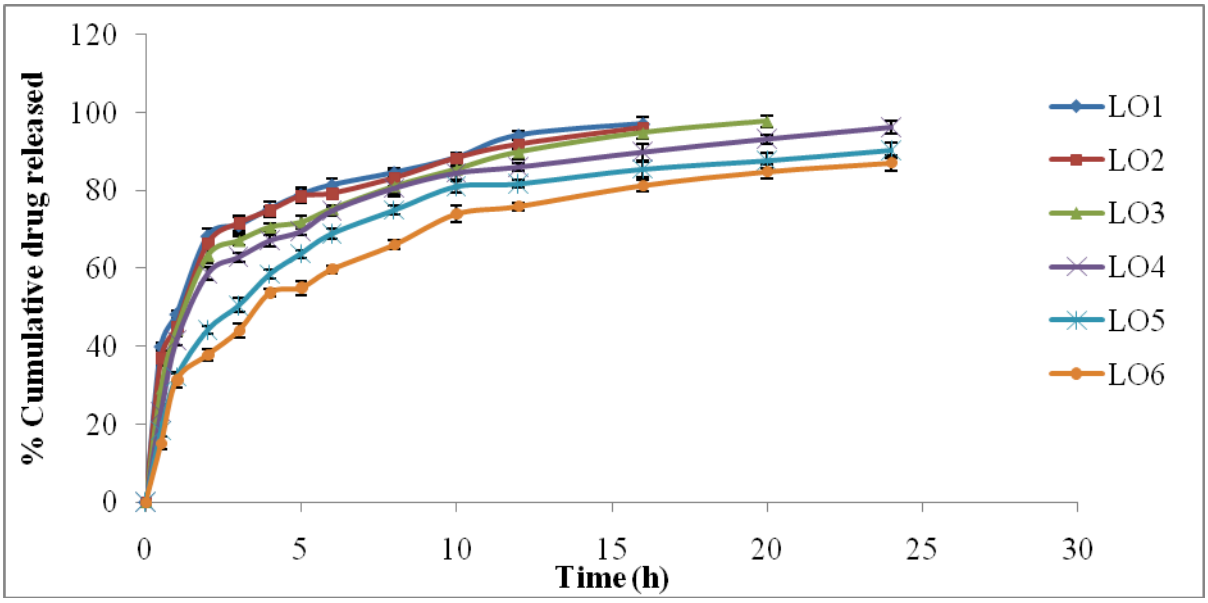

Figure 5: *In-Vitro* release profile of lamivudine loaded microspheres from different batches

Several factors such as surfactant concentration, volume of processing medium and stirring speed for emulsification process govern the drug release from the microspheres. As the concentration of the surfactant increased a faster drug release was observed as shown in the figure 6. This may be attributed to the presence of freer drug on the surface of the microspheres due to the decreased interfacial tension between the resin solution containing drug and processing medium, with increasing concentration of surfactant used for emulsification process. The difference was statistically significant ($P < 0.05$) for the formulations prepared at different surfactant concentrations.

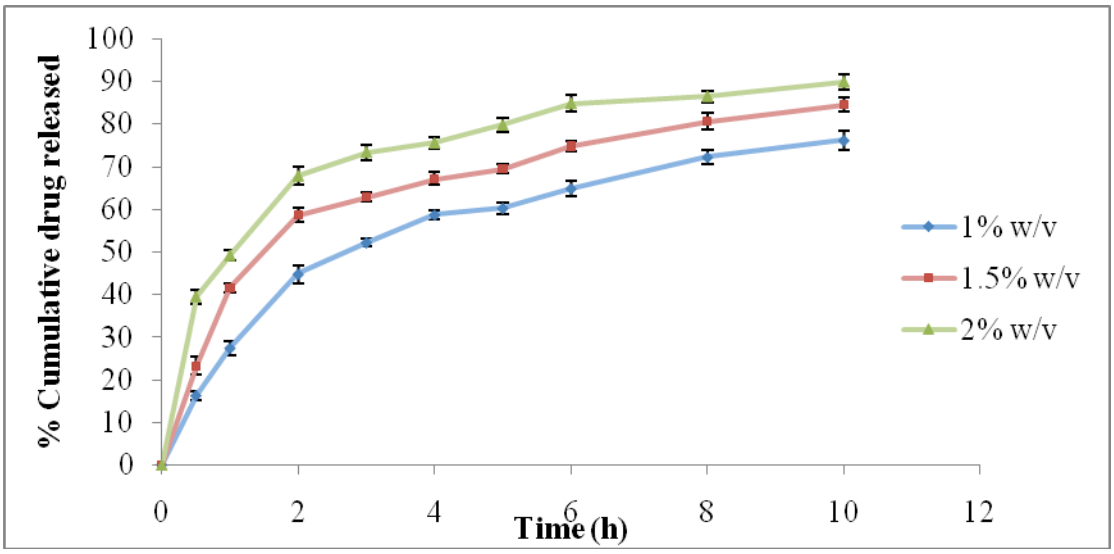

Figure 6: Effect of surfactant concentration on *in-vitro* drug release from microspheres of LO4 batch

The change in the volume of the processing medium has also influenced the drug release to a large extent as shown in the figure 7. It was observed that larger volume of the processing medium shows higher amount of the drug release as compared to the lower volume of the processing medium. This may be due to the fact that higher migration of the drug particles to the surface of the microspheres at larger volume of the processing medium during solvent evaporation process from freely moved emulsion droplets. The difference was statistically significant ($P < 0.05$). The best release was observed for formulation LO4, when the volume of the processing medium was 200ml as it was able to release around 96% of the drug within 24 hrs (Figure 5).

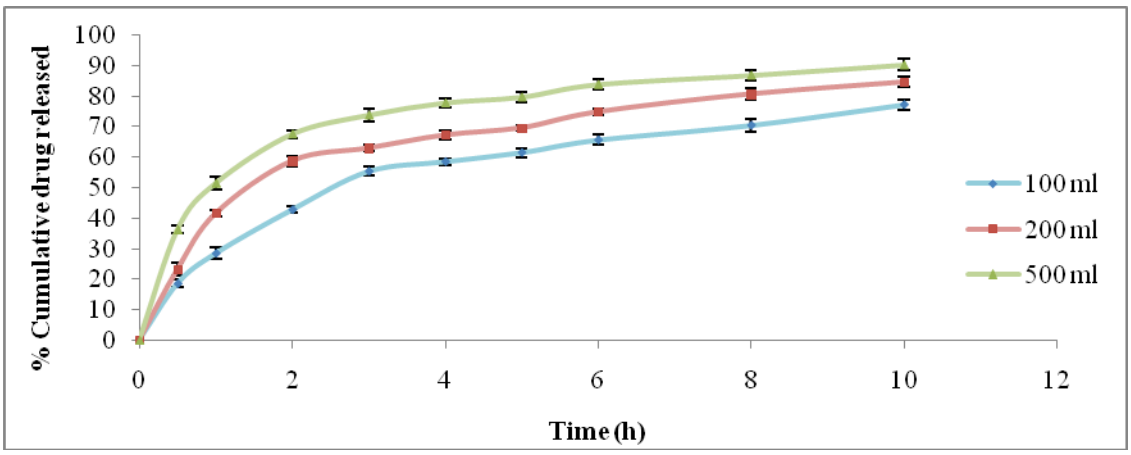

Figure 7: Effect of volume of the processing medium on *in-vitro* drug release from microspheres of LO4 batch

The change of the stirring speed of the emulsification process also influenced the drug release behavior from microspheres as shown in the figure 8, with a statistically significant difference ($P < 0.05$). It was observed that the amount of drug release decreases at higher rate of stirring. This may be due to the fact that less amount of the drug leaches out on to the microsphere surface at higher rate of stirring. However with a stirring speed of 1000rpm best release was observed for the formulation LO4.

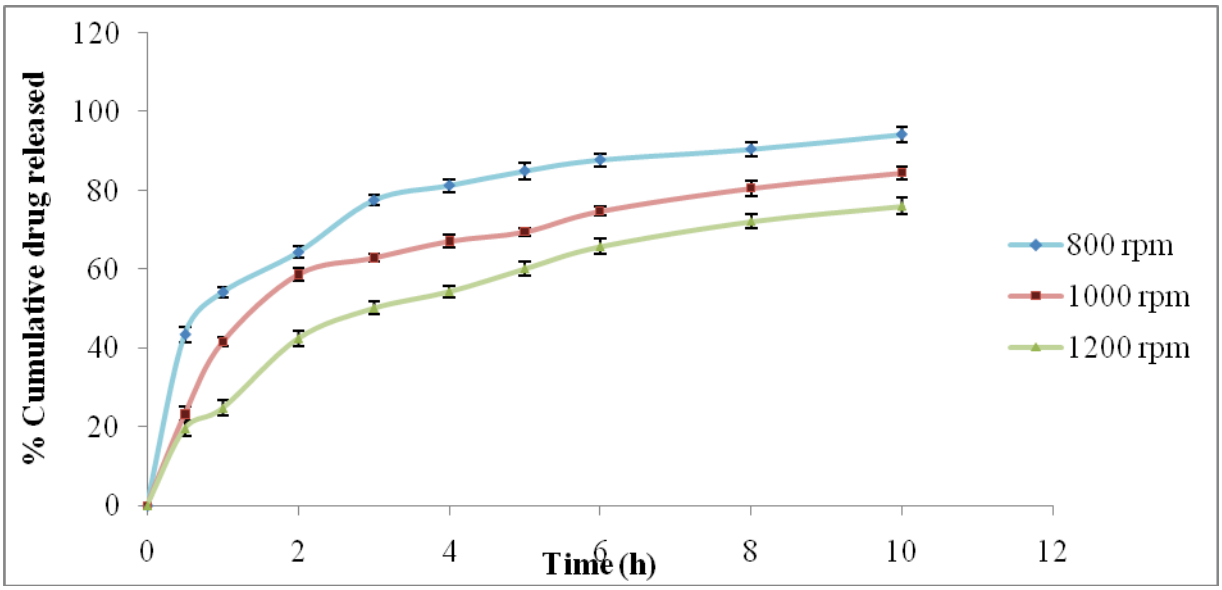

Figure 8: Effect of stirring speed on *in-vitro* drug release from microspheres of LO4 batch

Release kinetics

In order to evaluate the mechanism of drug release, various kinetic models like zero order, first order, Higuchi etc. were applied to the release profiles. The best fit with higher 'R^2' (coefficients of determination) value was obtained for first order then Higuchi and followed by zero order after linearization of the release results (table 3). As a high correlation was seen forfirst-orderthan that of Higuchi and zero-order kinetics, it confirms that the release was diffusion controlled and dependent on the concentration gradient between the dissolution medium and the microspheres. The diffusion coefficient '*n*' values, which describes the drug release mechanism wereestimated from the Korsemeyer-Peppas model. The '*n*'values of microspheres of different formulated batches were between0.252-0.413 (< 0.43), indicating Fickian diffusion mechanism.

Table 4: I*n-vitro* release kinetic parameters of lamivudine-loaded olibanum microspheres

Formulation codes	Zero order		First order		Higuchi model		Korsemeyerpeppas model
	R^2	K_0 (%/h)	R^2	K (h^{-1})	R^2	K_h (%/$h^{1/2}$)	*N*
LO1	0.615	4.326	0.955	0.191	0.855	21.53	0.252
LO2	0.62	4.35	0.946	0.175	0.859	21.63	0.27
LO3	0.644	3.59	0.971	0.165	0.873	19.83	0.298
LO4	0.623	2.915	0.95	0.119	0.857	17.88	0.321
LO5	0.683	3.036	0.909	0.092	0.902	18.25	0.388
LO6	0.741	3.042	0.942	0.08	0.941	17.8	0.413

CONCLUSIONS

Finally from the recent investigation it can be concluded thatuse of olibanum resin as controlled release microencapsulating agent for design of microspheres was successful. Industrially feasible methods of microencapsulation by the resins and gum could be developed as includes both emulsification and solvent evaporation method.Being natural resin is non-toxic, abundantly available, biodegradable and comparatively economical than various available synthetic polymers. Further investigationscan be augmented in the area of sustained or controlled release tablets, bio/mucoadhesive drug delivery systems, target specific drug delivery systems etc. by considering olibanum resin in future.

ACKNOWLEDGEMENTS

The author is very much thankful to the principal and governing body of Institute of Pharmacy & Technology, Salipur for providing every facility to carry out this work smoothly.

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