RESEARCH ARTICLE

Formulation and Evaluation of Pressed Coated Tablet Containing Combination of Fast Dissolving Lidocaine and Long Lasting Acyclovir Lozenge

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ABSTRACT

In this study, a press-coated tablet containing a combination of acyclovir (ACV) lozenge as an inner core and a fast-dissolving lidocaine layer as a coat was prepared in an attempt to provide an initial local anesthetic effect of lidocaine during the treatment of viral infection by ACV lozenges. The press-coated tablet was prepared by directly compressing the best ACV lozenges formulation followed by placing powder of fast dissolving lidocaine under and above the surface of the prepared ACV lozenge in the die of the tableting machine. Then all are compressed lightly. The pressed coated tablets were prepared, and their hardness, thickness, disintegration, and *in vitro* release of ACV and lidocaine were evaluated. The high-performance liquid chromatography-ultraviolet (HPLC-UV) detection was used for determining the contents of the two drugs in the pressed coated tablets. FTIR spectrophotometry analysis showed that there were no drug-drug and/or drug-excipient interactions indicating compatibility of the two drugs and excipients used in the formulation of the press-coated tablets. It was concluded that the press coated tablet is a promising dosage form to give fast release lidocaine and sustained release of ACV without any incompatibility problems.

Keywords: Acyclovir, Fast dissolving tablet, Lidocaine, Lozenges, Press coated tablet.

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INTRODUCTION

Multiple compressed tablets bring two or more compatible or incompatible materials together within the same tablet. Multiple compressed tablets can be divided into Layered tablets, which are either of two or three layers tablets, and compression coated tablets, which are of two types: tablet within tablet and tablet within tablet within a tablet.

Compression-coated tablets have two components, inner core and surrounding coat[1] Frequently, the coat is soluble in water and disintegrates without difficulty after swallowing.

The advantages of compressed coated tablet technology are the followings:

- It is easy and inexpensive.
- It is used for separating incompatible ingredients
- It could be used for making modified-release products like a delayed release to release the drug in the intestine.
- It is not harmful to the environment, as it does not need a high level of organic solvents.
- Compression-coated tablets may also be used to avoid pharmacokinetic interactions between drugs administered simultaneously, resulting in time between their releases into the gastrointestinal tract.
- The steps used in the production of the press-coated tablet are shown in Figure 1.

MATERIAL AND METHOD

Material

Lidocaine HCL and ACV powder were obtained from Wuxi Hexia, Chemical Company, China. Crospovidone (CP), croscarmellose sodium (CCS), mannitol, acacia, and all other materials are obtained through commercial sources.

Instrumentation

UV-Vis Spectrophotometer, Movel scientific instrument Co. Ltd. China; fourier transform infrared spectroscopy (FTIR),

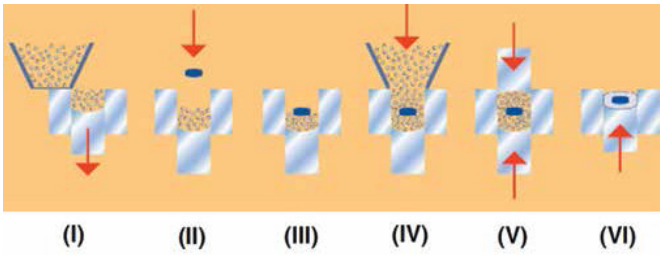

Figure 1: Procedure of press coating[2]

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Shimadzu 1650 pc-Japan; Disintegration apparatus LB-2D India; Dissolution apparatus, Copley-UK; Hotplate Stirrer; Dragon Lab-USA; PH meter Oahu's Corporation (USA); Electronic Balance, Kern ALS 220-4n-Germany; Electrical melting point apparatus, Stuart, Copley scientific, UK.

Preparation of Press-coated Table

Nine formulations of tableted lozenges of ACV and four formulations of lidocaine fast dissolving tablets (FDTs) were first prepared, and their compressibility and post-compression tests were evaluated. The optimum ACV lozenge formula (LOZ) and optimum lidocaine fast dissolving tablet formula (FT) shown in Tables 1 and 2, respectively were selected to prepare the press-coated tablet.[3] Approximately half the quantity of FT powder was placed first in the 12 mm diameter die of the single punch tablet machine. Then the ACV compressed tableted lozenge previously prepared from the optimum formula LOZ was put upon the FT powder in the center of the die. Then the remaining half quantity of the FT powder was added above the tableted lozenge, and all were compressed lightly together to obtain press coated tablet of 700 mg total weight.

Evaluation of the Prepared Press Coated Tablets

Weight Variation[4]

Ten tablets were arbitrarily selected and the average weight of these tablets was calculated after that the tablets were separately weighed and percent variation from the average was determined.

Thickness[4]

The thickness of tablets was measured individually for ten tablets by using vernier capillaries. The average thickness and standard deviation were recorded.

Tablet Hardness[5]

The hardness test of tablets was obtained by using Erweka hardness tester; the hardness of tablets was calculated in terms of kg/cm^2. Three tablets were selected randomly and tested for hardness. The average hardness of three tablet determinations was calculated.

***In vitro* Disintegration Test**[6,7]

Disintegration time of core tablets was found out by the mean of the tablet disintegration test apparatus, using 900 mL of phosphate buffer of pH 6.8 (as immersion medium) and maintained at 37ºC and the time measured for complete disintegration of the tablet with no tangible residue remaining on the screen was documented.

Drug Content

Determination drug content for a press-coated tablet was down by using HPLC Model (SYKAMN) Germane, Mobile phase = acetonitrile: phosphate buffer: (12:88) adjusted with pH = 4.1, Column = C18 – ODS (25cm * 4.6 mm), Detector = UV–210 nm, Flow rate = 1.3 mL/min.[8] Different concentrations of the active pharmaceutical ingredient in the physical mixture of formula D* were injected together with known concentrations of the standard, and the mean peak area ratios MPAR were documented. Calibration graphs of MPAR against a concentration of each drug was plotted to relate peak area ratios to concentrations. The real concentrations of the two drugs were interpolated from the required calibration graphs using the particular MPAR. Likewise, the recovery was achieved by injecting mixtures containing known concentrations of the two drugs and the standard of each drug, and the MPAR was used to confirm the concentrations of the two drugs.[9]

***In-vitro* Drug dissolution Study**[10]

The dissolution test of press coated tablet was carried out using phosphate buffer pH 6.8 as dissolution medium. Initially, press coated tablet was placed in 50 mL of dissolution media placed in 100 mL beaker placed on a hot pleat magnetic stirrer maintained at 37ºC and 50 rpm stirring rate. Five mL sample was withdrawn every minutes. and replaced with fresh dissolution media until the coat layer was completely dissolved. Later on the core tablet was moved to the jar of USP dissolution containing 250 mL fresh dissolution medium maintained at 37ºC and rotated at 50 rpm. Every 5 minutes five ml sample was withdrawn and replaced by 5 mL fresh dissolution media. All withdrawn samples were subjected to analysis for amounts of drugs released using UV-visible spectrophotometer at λmax of lidocaine for the samples of the coat and at λmax of ACV for the samples of the core of the press-coated tablet.

RESULT AND DISCUSSION

The results of compressed tablet lozenges perversely prepared from optimum formula (LOZ) were shown in Table 3. The weight variation test was within the pharmacopeia requirement limits (± 5). It was found to be 294.5.[11,12] Friability was 0.4% and met the stander friability criteria. So that the compressed tablet lozenge was expected to show satisfactory strength and withstand abrasion through handling and packaging.[13] The hardness test showed a value of 9.7 Kg/cm^2 within acceptable pharmacopeia limits.[14] The thickness was found to be 3.63 ± 0.2 mm which displays uniform thickness owing to

Table 1: Composition of the best formula of ACV compressed tableted lozenge

Formulation Code	*Drug (mg)*	*Sucrose (mg)*	*Concentration of acacia solution*	*Talc (mg)*	*Mg stearate (mg)*	*Color*	*Flavor*	*Total weight (mg)*
LOZ	200	97	10%	1.5	1.5	q.s	q.s.	300

Table 2: Composition of a best formula of lidocaine fast dissolving tablets best formula

Formulation Code	*Drug (mg)*	*CP*	*MCC*	*Aspartame (mg)*	*Mannitol (mg)*	*Talc (mg)*	*Mg Steaeate*	*Total weight (mg)*
FT	8	5%	120	12	232	4	4	400

Table 3: Post compression parameter of ACV compressed lozenges formula

Formula code	*Thickness (mm) n = 15*	*Hardness (Kg/cm²) ± S.D. * n = 3*	*Friability (%) n=10*	*In Vitro Disintegration Time (min) ±S.D.* n = 2*
LOZ	3.63±0.2	9.7	0.4	14 ±0.05

Table 4: Post compression parameters of lidocaine FT formula

Formula code	*Hardness (Kg/cm²) ± S.D.**	*Friability (%)*	*Wetting time (sec) ± S.D.**	*In vitro disintegration times (sec) ± S.D.**
FT	6.65 ± 0.0501	0.42	1.2± 20	32 ± 0.5

Table 5: Drug content for press-coated tablet for formula D* by using HPLC method.

No.	*St (mg / 700 mg*	*St (mg / gm.)*	*Con. (mg/gm.)*
Lidocaine	8	11.4	11.3
Acyclovir	200	278.1	275.8

(St); stander of drug, (Con); concentration of drug in press coated tablet

uniform die fill. The disintegration time of ACV compressed tablet lozenges best formula was 14 ± 0.05 min.

On the other hand, the results data for the optimum formula of lidocaine (FT) in Table 4 showed friability of less than 1%. They met the stander friability criteria giving an indication of good mechanical resistance of the tablets.[15] The hardness was found to be from 6.65 ± 0.05 kg /cm² indicating good mechanical strength with sufficient hardness.[16] The disintegration time was found 32 ± 0.5 sec, which complies with the test according to USP[11]. The wetting time of fast dissolving tablet was found to be 32 ± 0.5 sec.

Evaluation of press coated tablets showed average tablet weight of (690.5 mg ± 5%)[2] and hardness of 6.45 ± 0.2 kg/cm[2], and according to the reported data,[17] these values indicated good mechanical strength with appropriate hardness of the tablet and acceptable average weight. The thickness and diameter of the press-coated tablet were 6.8 mm and 12 mm respectively, indicating that the prepared tablets have uniform thickness and diameter as a result of uniform die fill.[18] Compared to the core tablet's result, it is clear that the increase in thickness is about 3.17 mm due amount of the coating layer of lidocaine formula powder. While the hardness of the press-coated tablet was less than that of compressed-coated lozenges, this may be attributed to additional compression applied for preparing press-coated tablet.

Evaluation of the two-drug content was performed using HPLC; the results showed that the percentage of ACV in the core of the tablet equal to 96.5%, while the percentage for lidocaine in the coating layer was 98.8%, indicating an accurate content of drugs. The method of analysis using reversed-phase HPLC can precisely determine the two drug contents both in the press coated tablet or physical mixture of formula D* as shown in Figures 2A-C). It complies with official specifications.[20]

In vitro Dissolution of Press-coated Tablet

The results of in vitro dissolution of press coated tablet showed that 95.8% of ACV was released from the core tablet after 35 minutes (Figure 3), which is approximately similar to the dissolution profile of ACV compressed tableted lozenge of

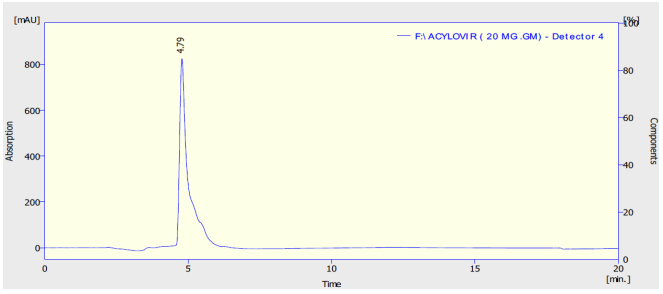

Figure 2 A: HPLC-UV detection of acyclovir pure drug

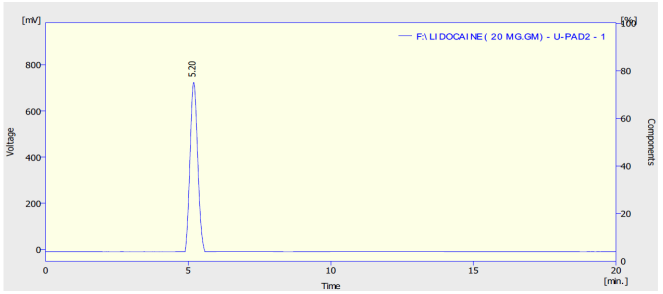

Figure 2 B: HPLC-UV detection of lidocaine pure

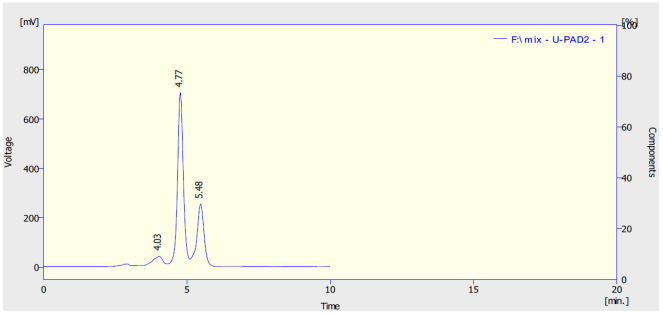

Figure 2C: HPLC-UV detection of a physical mix of lidocaine and acyclovir

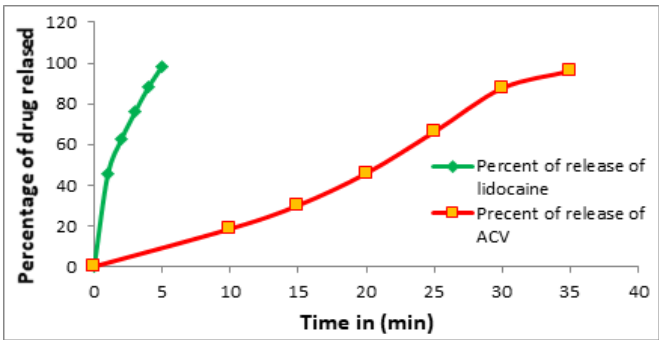

Figure 3: the dissolution profile of press-coated tablet formula D* in phosphate buffer (pH 6.8) at 37ºC ± 0.5ºC and 50 rpm.

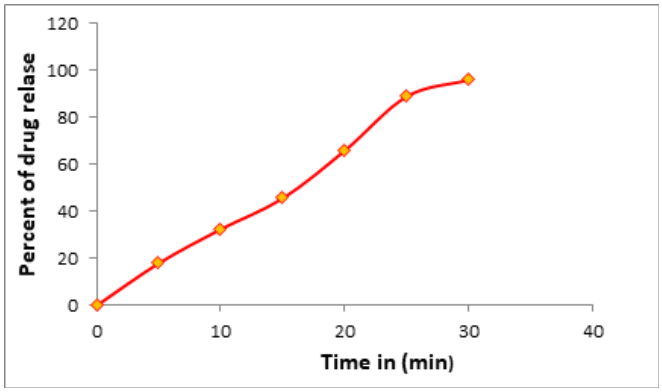

Figure 4: The dissolution profile of the prepared ACV compressed tablet lozenges of optimum formula (LOZ) in phosphate buffer (pH 6.8) at 37ºC ± 0.5 ºC and 50 rpm.

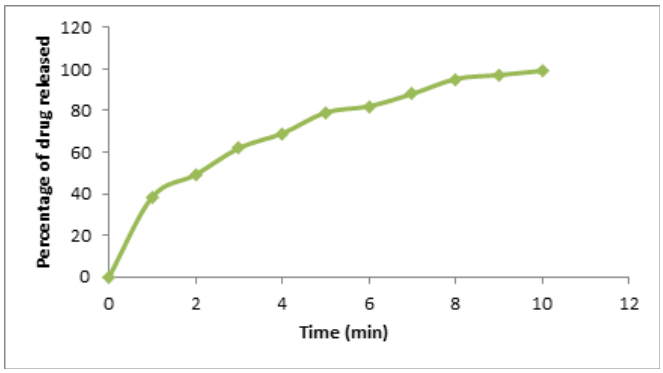

Figure 5: The dissolution profile of the fast dissolving tablet of lidocaine best formula (FT) in phosphate buffer (pH 6.8) at 37ºC ± 0.5ºC and 50 rpm.

optimum formula as shown in Figure 4. The percentage of ACV released from the selected formula was 96% after 30 minutes. The results indicated that the press-coated tablet could be used to give the same duration effect of ACV as that obtained with the tableted lozenge of the drug.

The percentage of lidocaine released from the coating layer of the press-coated tablet showed 98.5% after 5 minutes. The optimum formula of fast dissolving table required 10 minutes to release the same amount of drug as shown in Figure 5. This faster dissolution is attributed to lightly compression of the coating layer during press-coated tablet preparation. This fast release of lidocaine is important for producing a fast local anesthetic effect. Hence, the faster drug release can be associated with the high disintegration due to decrease particle contact between each other. The effect of the decreased relative surface area of tablet following in an overall increased absolute drug release rate.[21]

CONCLUSION

From the results of this study, it can be concluded that press-coated tablets could be used to give fast lidocaine release, which is essential for relieving the pain associated with viral infection through the local anesthetic affect and to obtain a continuous release of ACV from the core of the press-coated tablets.

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