

Solubility and Dissolution Enhancement of Atorvastatin Calcium using Solid Dispersion Adsorbate Technique

Samer K. Ali*¹ and Eman B. H. Al-Khedairy*

*Department of Pharmaceutics College of Pharmacy, University of Baghdad, Baghdad, Iraq.

Abstract

Atorvastatin (ATR) is a poorly soluble anti-hyperlipidemic drug. The drug belongs to the class II group according to the biopharmaceutical classification system (BCS) with low bioavailability due to its low solubility. Solid dispersions adsorbate is an effective technique for enhancing the solubility and dissolution of poorly soluble drugs.

The present study aims to enhance the solubility and dissolution rate of ATR using solid dispersion adsorbate technique in comparison with ordinary solid dispersion. polyethylene glycol 4000 (PEG 4000), polyethylene glycol 6000 (PEG 6000), Poloxamer188 and Poloxamer 407 were used as hydrophilic carriers besides Aerosil 200, Aerosil 300 and magnesium aluminium silicate (MAS) as adsorbents.

All solid dispersion adsorbate (SDA) formulas were prepared in ratios of 1:1:1 (drug: carrier: adsorbent) and evaluated for their water solubility, percentage yield, drug content, dissolution, crystal lattice using X-ray powder diffraction (XRD) and Differential Scanning Calorimetry (DSC) studies and Fourier Transform Infrared Spectroscopy (FTIR) for determination the drug-carrier- adsorbate interaction.

The prepared (SDA) showed improvement of drug solubility in all prepared formula. The best result was obtained with formula SDA12 (ATR: Poloxamer407: MAS 1:1:1) that showed 8.07 and 5.38 fold increase in solubility compared to solubility of pure ATR and solid dispersion(SD4) (Atorvastatin: Poloxamer 407 1:1) respectively due to increased wettability and reduced crystallinity of the drug which leads to improving drug solubility and dissolution.

Keywords: Atorvastatin , Solid dispersions adsorbate, PEG4000 and 6000, Aerosil 300 , Magnesium aluminium silicate

تحسين الذوبانية ومعدل الذوبان للاتروفستاتين كالمسيوم باستخدام تقنية الصلب المنتشر الممتز

سامر خالد علي*^١ و ايمان بكر حازم الخضيرى*

*فرع الصيدلانيات، كلية الصيدلة، جامعة بغداد، بغداد، العراق .

الخلاصة

الأتروفستاتين هو دواء مضاد لارتفاع الدهون في الدم و قليل الذوبان ؛ و ينتمي إلى مجموعة الصنف الثاني طبقاً لتصنيف المستحضرات الصيدلانية الحيوية و الذي يتميز بضعف التوافر الحيوي بسبب قلة ذوبانه. الصلب المنتشر الممتز هو طريقة فعالة لتعزيز قابلية ومعدل الذوبان للادوية قليلة الذوبان.

الهدف من هذه الدراسة الحالية هو تحسين قابلية ومعدل الذوبان لدواء الأتروفستاتين باستخدام تقنية الصلب المنتشر الممتز ومقارنته مع الصلب المنتشر العادي. حيث تم استخدام البولي إيثيلين كليكول ٤٠٠٠ ، البولي إيثيلين كليكول ٦٠٠٠، بولكسمر ١٨٨ و بولكسمر ٤٠٧ كناقلاات محبة للماء والايروسيل ٢٠٠، الايروسيل ٣٠٠، سليكات المغنيسيوم والألومنيوم كموات ممتزة .

تم تحضير جميع صيغ الصلب المنتشر الممتز بنسب ١ : ١ : ١ (دواء: ناقل: ممتز) وتم تقييمها حسب قابلية الذوبان في الماء والنسبة المئوية المستحصلة ، ومحتوى الدواء، معدل الذوبان ، والهيكل البلوري باستخدام تقنية حيود الأشعة السينية ومسعر المسح التبايني و مطياف الأشعة تحت الحمراء لتحديد التفاعل الحاصل بين الناقل والممتز والدواء.

ولقد اظهرت النتائج تحسن في قابلية الذوبان للدواء في جميع الصيغ المحضرة بتقنية الصلب المنتشر الممتز. وتم الحصول على افضل نتيجة بالصيغة SDA12 (أتروفستاتين : بولكسمر ٤٠٧ : سليكات المغنيسيوم والألومنيوم ١ : ١ : ١) التي اظهرت زيادة بنسبة ٨,٠٧ و ٥,٣٨ ضعف في الذوبانية مقارنة بذبوان الأتروفستاتين النقي والصلب المنتشر العادي على التوالي بسبب زيادة قابلية البلل وانخفاض الحالة البلورية للدواء مما يؤدي الى زيادة قابلية الذوبان ومعدل الذوبان في الدواء.

الكلمات المفتاحية: الأتروفستاتين ، الصلب المنتشر الممتز، بولي اثلين كيكلول ٤٠٠٠ و ٦٠٠٠، ايروسيل ٣٠٠، سليكات المغنيسيوم والألومنيوم.

Introduction

The solubility of drug molecules is a significant determinant of the dissolution rate because of dissolution rate is closely tied to solubility⁽¹⁾. Poor solubility and low dissolution rate of poorly water - soluble drugs in the aqueous gastrointestinal fluids often cause poor

bioavailability, Principally for class II drugs, the enhancement of the solubility and dissolution rate of the drug in the gastrointestinal fluids may improve the bioavailability, For BCS class II drugs, the release from the dosage form and solubility in the gastric fluid are the rate-limiting steps rather than their absorption⁽²⁾.

¹Corresponding author E-mail: samerkhalidali@gmail.com

Received: 26 / 5 /2019

Accepted: 3 / 8 /2019

Atorvastatin calcium (ATR) is $[C_{33}H_{35}FN_2O_5]_2 \cdot Ca \cdot 3H_2O$ as an empirical formula, and Chemical structure is shown in figure 1⁽³⁾.

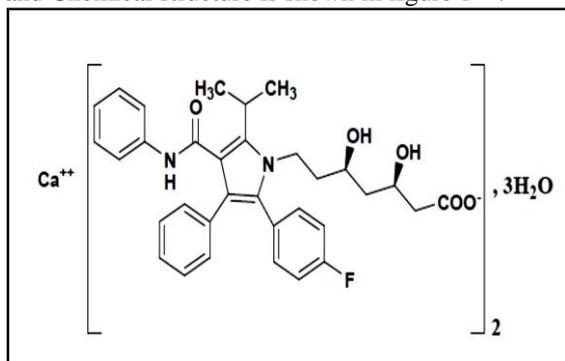


Figure 1. Chemical structure of atorvastatin calcium⁽³⁾

Atorvastatin calcium (ATR) is an antihyperlipidemic agent able to lowering blood cholesterol levels by the reversible inhibition of HMG-CoA reductase, a rate-limiting step in the cholesterol biosynthesis. It represents one of the most widely administered oral statins used in case of elevated plasma levels of cholesterol, triglycerides, low-density lipoproteins in addition to its ability to elevate the high-density lipoproteins⁽⁴⁾. ATR belongs to BCS class II drug⁽⁵⁾. The drug is very slightly soluble in distilled water with the pKa value of 4.46 and Log p values of 6.36 in octanol/water. It has an absolute oral bioavailability of 12 %. The poor oral bioavailability is attributed to presystemic clearance in the gastrointestinal mucosa and high hepatic first-pass metabolism⁽⁶⁾. Many authors have worked to improve the solubility and dissolution rate of ATR by preparing microsphere, emulsion, nanosuspension, self- microemulsion, solid dispersion⁽⁷⁾.

Solid dispersion (SD) is the most generally used technique for bioavailability enhancement of poorly water-soluble drugs, as the drug dispersed in freely soluble carrier⁽⁸⁾.

Some difficulties limiting the commercial use of solid dispersion such as; formulation into dosage forms (Poor flow, poor compressibility and a requirement of a large quantity of carrier), the scale-up of production processes. In addition, phase separation, crystal growth during storage are also considered to be significant problems to commercialise solid dispersions since the solubility and hence dissolution rate may be decreased during storage^(9,10).

Solid dispersion adsorbate (SDA) is a technique in which SD is adsorbed onto hydrophilic adsorbent which has an exceedingly high surface area to form a free-flowing powder and to achieve improved solubility, dissolution rates and hence bioavailability⁽¹¹⁾.

The effect of adsorbent will help in commercialisation of SD as a tablet or capsule dosage form by improving poor compressibility by

adsorbing the SD onto a free-flowing carrier. On the other hand, the stability problem can be reduced by the use of novel excipient like Neusilin® which along with improving the flow property also inhibits the conversion of amorphous form back to the crystalline form by entrapping the molecularly dispersed drug into its porous network⁽¹²⁾. Other adsorbents were also used, including Aerosil, Florite, and Sylvania having different characteristics such as particle size, pore size, and specific surface area⁽¹³⁾.

The aim of this study was to enhance the solubility and dissolution rate of ATR by solid dispersion adsorbate technique using Polyethylene glycol (PEG)4000 and 6000 or poloxamer188 and 407 as a hydrophilic carrier and Magnesium aluminium silicate (MAS) or Aerosil200 or Aerosil 300 as adsorbents.

Materials and Method

Materials

Atorvastatin calcium (ATR), Aerosil200 and PEG 6000 were supplied by Pioneer pharmaceutical company, Iraq as a gift sample. Poloxamer188, poloxamer407, Magnesium aluminium silicate (MAS) and aerosil300 were purchased from Hangzhou, Hyperchem. China. PEG 4000 was purchased CDH, India.

Method

Preparation of solid dispersion of atorvastatin calcium

Solid dispersions of ATR were prepared using a melting method. In this method, the carrier (PEG4000, PEG 6000, Poloxamer 188 or poloxamer 407) is melted using water bath at its corresponding melting point, and the drug was then incorporated into the molten carrier mass in a ratio of 1:1 with constant stirring. The blend was cooled at room temperature. The solid dispersion was pulverised through a 60 mesh sieve and stored in the desiccator for further use⁽¹⁴⁾. The prepared solid dispersions are shown in table 1.

Preparation of solid dispersion adsorbate (SDA) of atorvastatin calcium

Solid dispersion adsorbate of ATR was prepared by addition of the drug to melt of each carrier individually in porcelain dish on a water bath at 60°C and mixed. Once homogeneous slurry was obtained, the adsorbent (Aerosil 200, Aerosil 300 or MAS.) was added and stirred until the blend was converted to mass. The drug to a carrier to adsorbent ratio was fixed at 1:1:1 (Table 2). Finally, the mass was allowed to cool at room temperature. The SDAs were passed through a 60 mesh sieve to obtain a free-flowing powder of uniform size⁽¹⁵⁾.

Table 1. Composition of different SD formulas of ATR

Formula code	ATR (g.)	PEG4000 (g.)	PEG6000 (g.)	Poloxamer188 (g.)	Poloxamer407 (g.)
SD1	1	1
SD2	1	...	1
SD3	1	1	...
SD4	1	1

Preparation of physical mixture (PM)

The PM was prepared by uniform mixing of drug, carrier and adsorbent in the same ratios of

SDA. The mixing powder was passed through a sieve 60 mesh to get uniformly sized particles⁽¹⁶⁾.

Table 2. Composition of different SDA formulas of ATR.

Formula name	ATR (g.)	PEG 4000 (g.)	PEG 6000 (g.)	Poloxamer 188 (g.)	Poloxamer 407 (g.)	Aerosil200 (g.)	Aerosil 300 (g.)	MAS (g.)
SDA1	1	1	1
SDA2	1	1	1	...
SDA3	1	1	1
SDA4	1	...	1	1
SDA 5	1	...	1	1	...
SDA 6	1	...	1	1
SDA 7	1	1	...	1
SDA 8	1	1	1	...
SDA 9	1	1	1
SDA 10	1	1	1
SDA 11	1	1	...	1	...
SDA 12	1	1	1

Evaluation of SD and SDA**Determination of saturation solubility**

An excess amount of ATR, SD and SDA were added to 10 ml of water; the samples were incubated in water bath shaker at 25 °C for 48 hr. after that, the samples were filtered through a 0.45µm syringe filter and diluted when necessary. The diluted samples were analysed by UV spectrophotometer at 241 nm was used to determine the dissolved quantity of atorvastatin⁽¹⁷⁾.

Determination of percentage yield (PY %)

The Percentage yield was measured for each type of SD and SDA, which was calculated using equation 1⁽¹⁸⁾.

$$PY\% = \frac{\text{Actual weight of SD or SDA}}{\text{Theoretical weight of SD or SDA}} \times 100 \quad (1)$$

Determination of drug content of SD and SDA

An accurately weighed quantity of SD and SDA equivalent to 10mg of ATR was taken and dissolved in a 10 ml of methanol and volume was made up to 50 ml. From this, 1ml of the solution was taken and further diluted ten times with methanol. The solution was assayed for drug content using UV

spectrophotometry method by measuring the absorbance at 247 nm⁽¹⁹⁾. The percentage of drug content in the SD and SDA was calculated by using equation 2⁽²⁰⁾.

Drug content

$$\% = \frac{\text{Actually gained weight of ATR}}{\text{Theoretical weight of ATR}} \times 100 \quad (2)$$

In-vitro dissolution studies

In-vitro dissolution studies of SDA equivalent to 20mg atorvastatin were carried out in 900 ml phosphate buffer (pH 6.8) in USP apparatus-Type II (PHARMA TEST, Germany) at 37 ± 0.5 °C and 75 rpm⁽²¹⁾. Aliquots of 5 ml were withdrawn and then replaced by fresh media of dissolution at regular time intervals, filtered, and was analysed spectrophotometrically at 240nm by UV visible spectrophotometer (Cary win UV, Australia).

X-ray powder diffraction (XRD)

The X-ray powder diffraction spectra of optimised formula, PM, and ATR were recorded using Shimadzu X-diffractometer (Model: XRD-6000, Japan). Samples were pulverised into powders with a mortar and pestle, and the cross-section of

samples was exposed to x-ray radiation. The scanning angle ranged from 5 to 80 of 2θ , voltage-40kV and current - 40 mA⁽²²⁾.

Differential scanning calorimetry (DSC)

Differential scanning calorimetry of ATR, optimised formula, PM, carrier and adsorbent were done using DSC60 (Shimadzu, Japan). Thermal behaviour of the samples was investigated under a scanning rate of 10 °C/min, covering a temperature range of 20–200 °C under inert atmosphere flushed with nitrogen at a rate of 20 ml/min⁽²³⁾.

Fourier transform infrared (FTIR)

Fourier Transform Infrared spectra of ATR, MAS, PM and the optimized formula were obtained using Shimadzu, Fourier Transform Infrared Spectroscopy (FTIR 43000), (Japan), each sample was dispersed in KBr powder, blend well in mortar and pestle, and compressed into transparent discs for FTIR examination and FTIR spectra were recorded in spectra region 4000 to 400 cm^{-1} at an instrument resolution of 4 cm^{-1} ⁽²⁴⁾.

Results and Discussion

Saturation solubility of ATR SDs

Results of saturation solubility studies of ATR SDs are shown in table 3.

Table 3. The solubility of pure ATR and SDs formulas using different carriers with drug: carrier ratio 1:1 in distilled water at 25°C.

Formula Code	Carrier	Saturation solubility $\mu\text{g/ml}$ (Mean \pm STD) n=3
Pure ATR		120.2 \pm 0.013
SD1	PEG 4000	126.01 \pm 0.014
SD2	PEG 6000	129.95 \pm 0.012
SD3	Poloxamer 188	141.1 \pm 0.005
SD4	Poloxamer 407	180.34 \pm 0.017

Significant enhancement in solubility of ATR ($p < 0.05$) was obtained, which may be attributed to the hydrophilic nature of all the used carriers, besides hydrogen bonding that may be formed between ATR and carriers led to enhance the solubility of ATR⁽²⁵⁾. The solubility enhancement of the various carriers was found to be in the following descending order: poloxamer407 > poloxamer188 > PEG6000 > PEG4000. The highest solubility was obtained using poloxamer 407 as a carrier due to the surfactant effect of poloxamer 407 and micelles formation⁽²⁶⁾.

Saturation solubility of ATR SDAs

Table 4 shows the results of solubility ATR SDAs. Further improvement in solubility was obtained when ATR prepared as SDAs in comparison to that obtained by SDs. that can be explained to be due to

adsorption of ATR on the hydrophilic adsorbent and increase the surface area of ATR that exposed to the solvent, whereby the drug is bound to the adsorbent and thus cannot agglomerate which results in enhanced wettability of the drug particles and hence its solubility^(27,28).

Table 4. The solubility of ATR SDAs prepared with different adsorbents with drug : carrier: adsorbent ratio 1:1:1 in distilled water at 25°C.

Batch no.	Carrier: Adsorbent (1:1)	Saturation solubility $\mu\text{g/ml}$ (Mean \pm STD) n=3
SDA1	PEG4000:Aerosil 200	136.2 \pm 0.002
SDA 2	PEG4000:Aerosil 300	157.3 \pm 0.006
SDA 3	PEG4000:MAS	810.8 \pm 0.109
SDA 4	PEG6000:Aerosil 200	142.8 \pm 0.009
SDA 5	PEG6000:Aerosil 300	162.5 \pm 0.004
SDA 6	PEG6000:MAS	863.5 \pm 0.014
SDA 7	Poloxamer 188:Aerosil 200	149.5 \pm 0.057
SDA 8	Poloxamer 188:Aerosil 300	168.3 \pm 0.017
SDA 9	Poloxamer 188:MAS	880.5 \pm 0.024
SDA 10	Poloxamer 407:Aerosil 200	243.2 \pm 0.026
SDA 11	Poloxamer 407:Aerosil 300	280.2 \pm 0.027
SDA 12	Poloxamer 407:MAS	970.8 \pm 0.027

The solubility enhancement of the various adsorbents was found to be in the following descending order: **MAS > Aerosil 300 > Aerosil 200** in the presence of any hydrophilic carrier (figure 2). The results may be due to the difference adsorption capacity of three adsorbents to the drug. Highest solubility was obtained with MAS because it has excellent disintegrating activity in an aqueous solution⁽²⁹⁾ and large surface area due to its composition of many silicate layers and good adsorption properties because of a negative charge on the surface of the silicate layers that brings about a strong electrostatic interaction with a cationic drugs and the silanol groups can interact by

hydrogen bond with drugs which gives it good adsorption properties⁽³⁰⁾.

Whereas the difference adsorption capacity of two other adsorbents to the drug can be explained to the difference in their surface area as the surface area of Aerosil 300(300 ±30m²/g), so it has high adsorption capacity when compared with Aerosil 200(200 ± 25m²/g)⁽³¹⁾.

Therefore, the largest surface area of ATR that exposed to the dissolution medium was obtained when it is adsorbed on MAS.

Formula SDA12 showed the highest solubility 970.8±0.0274 µg/ml compared to 120.2±0.0138 µg/ml for pure drug and 180.34µg/ml solid dispersion(SD4) (ATR: Poloxamer407 1:1) indicating that solid dispersion adsorbate technique enhances the solubility by 8.07 and 5.38 fold as compared to the pure drug and ordinary SD respectively.

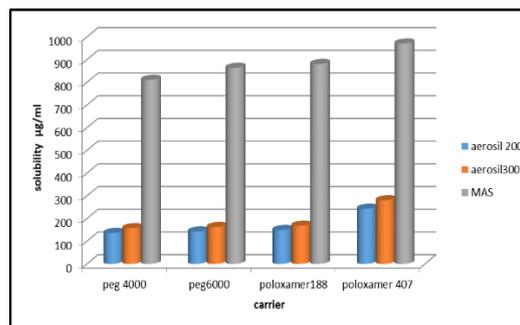


Figure2. Effect of adsorbent and carrier type of ATR SDA at ratio (1:1:1) on the solubility of ATR in distilled water at 25°C

Determination of percentage yield (PY %) and content of prepared SD and SDA

The prepared SDs and SDAs formulas showed high percentage yield ranged between 85.5-98.53%. This result indicating the suitability of the method (melting or melt adsorption method) with the used material for such preparations.

On the other hand, the drug content in all the formulations was found to be within 98-100% w/w, which is in agreement with U.S.P requirements (98-102%)⁽²¹⁾. The results of percentage yield and drug content are shown in table 5.

Table 5. Percentage yield and drug content of SD and SDA

Formula Code	Percentage yield (PY %)	Drug content (w/w) (%) (Mean ±STD) (n=3)	Formula Code	Percentage yield (PY %)	Drug content (w/w) (%) (Mean ±STD) (n=3)
SD1	93.71	98.10 ±0.06	SDA 5	97.26	99.45 ±0.06
SD2	85.50	98.08 ±0.01	SDA 6	93.73	98.67 ±0.02
SD3	95.98	99.34 ±0.05	SDA 7	90.66	98.02 ±0.04
SD4	96.85	98.59 ±0.03	SDA 8	96.86	98.70 ±0.04
SDA1	86.80	98.00 ±0.14	SDA 9	95.93	99.00 ±0.01
SDA2	94.26	99.23 ±0.03	SDA 10	98.53	98.03 ±0.02
SDA 3	90.40	99.10 ±0.02	SDA 11	98.00	99.10 ±0.02
SDA 4	91.13	98.4 ±0.05	SDA 12	97.93	100.00±0.01

In-vitro dissolution studies

Comparative *in-vitro* dissolution of the pure drug, SDA12 (ATR:poloxamer407: MAS 1:1:1),SD4(ATR:polxamer407 1:1)and physical mixture(PM) of SDA12 was studied

The similarity factor (*f*2) was used to consider similar dissolution profiles (equation 3).

$$f2 = 50 \times \log \left\{ \left[1 + \frac{1}{n} \sum_{t=1}^n |R_t - T_t|^2 \right]^{-0.5} \times 100 \right\} \dots \dots \text{Equation (3)}$$

Where (n) is the number of dissolution time points. (R_t) and (T_t) is the reference and test dissolution values at time t.

The two dissolution profiles consider similar when *f*2 values higher than 50 (50– 100); otherwise, the profiles are not similar⁽³²⁾.

An improvement in the dissolution was obtained (figure 3) by SDA12 in comparison with SD4 (*f*2=48.55), PM of SDA12 formula (*f*2=40.23) and pure drug (*f*2=27.26). This result can be due to increased solubility by the formation of hydrogen bonding between the drug and MAS, micellar solubilisation of ATR in poloxamer407, improved wettability and amorphisation of ATR⁽³³⁾. That needs further investigation by FTIR, XRD and DSC.

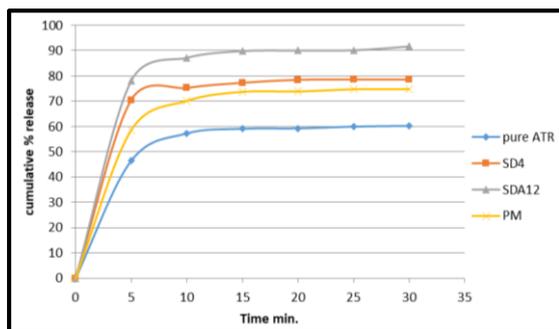


Figure 3. Comparative *in-vitro* dissolution profile of the ATR, SDA12, SD4 and physical mixture of SDA12 (PM) at phosphate buffer 6.8 and $37^{\circ}\text{C} \pm 0.5$

X-ray powder diffraction (XRD)

The XRD diffractogram of ATR, SDA 12 and PM are shown in Figure 4. The diffraction pattern of the pure drug showed characteristic high-intensity peaks at 9.06, 9.38, 10.17, 11.74, 16.89, 19.32, 21.48, 22.5549, 23.17 and 23.57, which indicates that the drug is present in the crystalline form that is also confirmed by DSC results. Physical mixture's pattern showed the characteristic peaks of ATR with lower intensity compared to the pure drug. This result can be explained to be due to the dilution effect of the carrier. In contrast, Further decrease or absence of the characteristic peaks of ATR was observed with SDA 12, indicating that an amorphous form mostly exists in solid dispersion adsorbate^(34,35). This amorphous form may contribute to solubility improvement since this form is more easily soluble than the crystalline form.

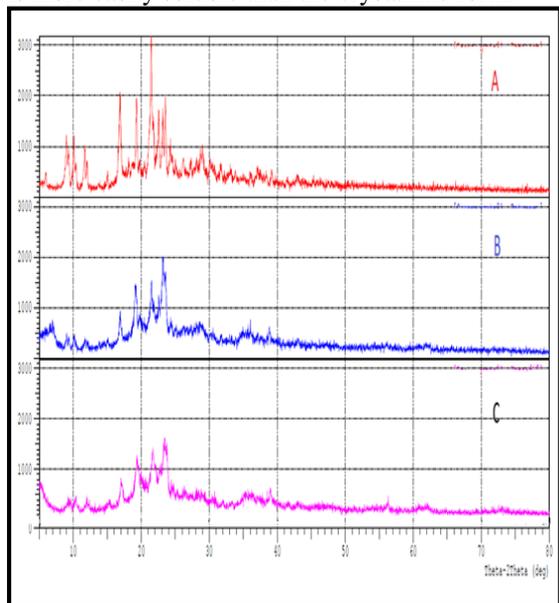


Figure 4. X-ray diffractograms of ATR (A), PM (B) and solid dispersion adsorbate of selected formula SDA12 (C)

Differential scanning calorimetry (DSC)

Thermograms of ATR, MAS, Poloxamer407, PM and the SDA12 are shown in figure 9, respectively. The DSC curve of ATR gives an endothermic peak corresponding to its melting point at 160.04°C ; the result indicated the purity and crystallinity of the used ATR.⁽⁶⁾ While the DSC of MAS shows no endothermic peak in the studied DSC temperature range and Poloxamer407 shows an endothermic peak at 53.80°C correspondings to its melting point⁽³⁶⁾. PM shows the only distinct peaks of Poloxamer407 with a decrease in intensity and melting point to 47.04°C which may be due to dilution with other components while the absence of ATR peak may be due to adsorption of the drug on MAS⁽³⁷⁾ which will be confirmed by FTIR study. The thermogram of SDA12 shows further decrease in the intensity of poloxamer 407 with disappearance of ATR peak which may be due to adsorption effect and its complete dispersion in the melted polymer and conversion of the drug from crystalline to amorphous state⁽³⁸⁾.

Fourier transform infrared (FTIR)

The ATR exhibits characteristic peaks at 3664cm^{-1} (free O–H stretching), 3365cm^{-1} (O–H stretching), 3278cm^{-1} and 3060cm^{-1} (N–H stretching multiple band), 2966cm^{-1} (C–H stretching), 1651cm^{-1} (amide C=O stretching), 1581cm^{-1} (aromatic C=OC stretching), 1516cm^{-1} (N–H bending), 812cm^{-1} (out of plane N-H wagging) were found in the crystalline form (Unprocessed drug) as shown in figure 6^(39,3). The FTIR Spectrum of PM showed the characteristic peak of ATR with low intensity indicates the predominant effect of carrier and adsorbent concentration⁽⁴⁰⁾.

The spectrum of the SDA15 showed broad and weak O–H stretch peak (3365cm^{-1}) and N–H stretching multiple bands compared to atorvastatin crystalline drug. Besides, a broad peak or absent peak corresponding to a hydroxyl stretching of MAS SiOH 3620cm^{-1} that may be due to the formation of a hydrogen bond between silanol group on the surface of MAS and hydroxyl group and amide group of ATR^(39,41).

The carboxyl stretching peaks at 1651 and 1581cm^{-1} of ATR shifted to higher wavenumber (1655 and 1589cm^{-1}) and presented lower intensity in SDA12 (figure 10, D), indicating an electrostatic interaction of carboxyl group of ATR with the positively charged sites in the edges of MAS structure⁽³⁷⁾.

The most characteristic peaks of ATR are still present but some decrease in intensity and shifting of some peak, this indicates that there was no chemical incompatibility between drug, carrier and adsorbate otherwise it confirm the adsorption process.

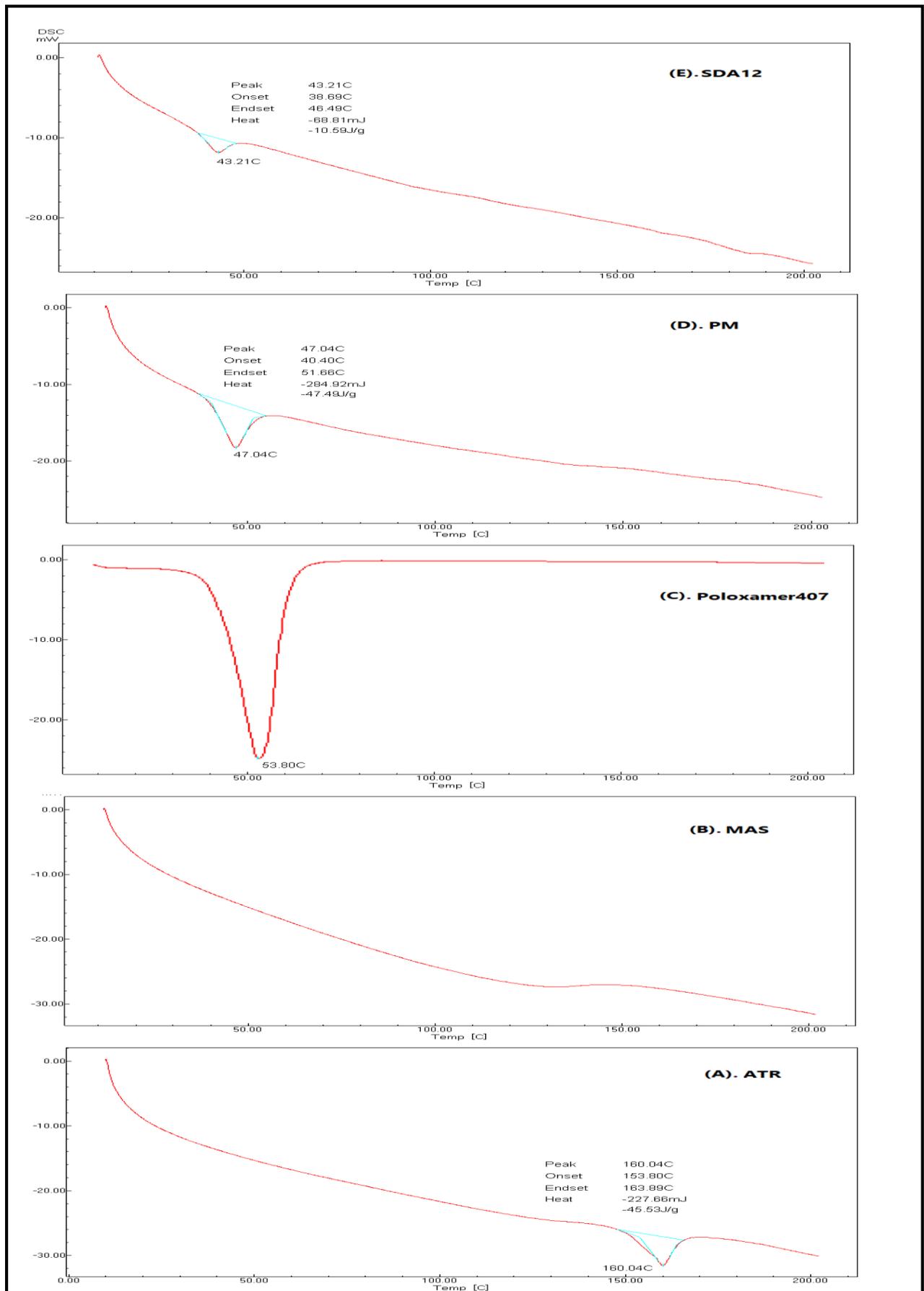


Figure 5. DSC: ATR(A) , MAS (B) , Poloxamer407(C), PM (D) , SDA12 (E)

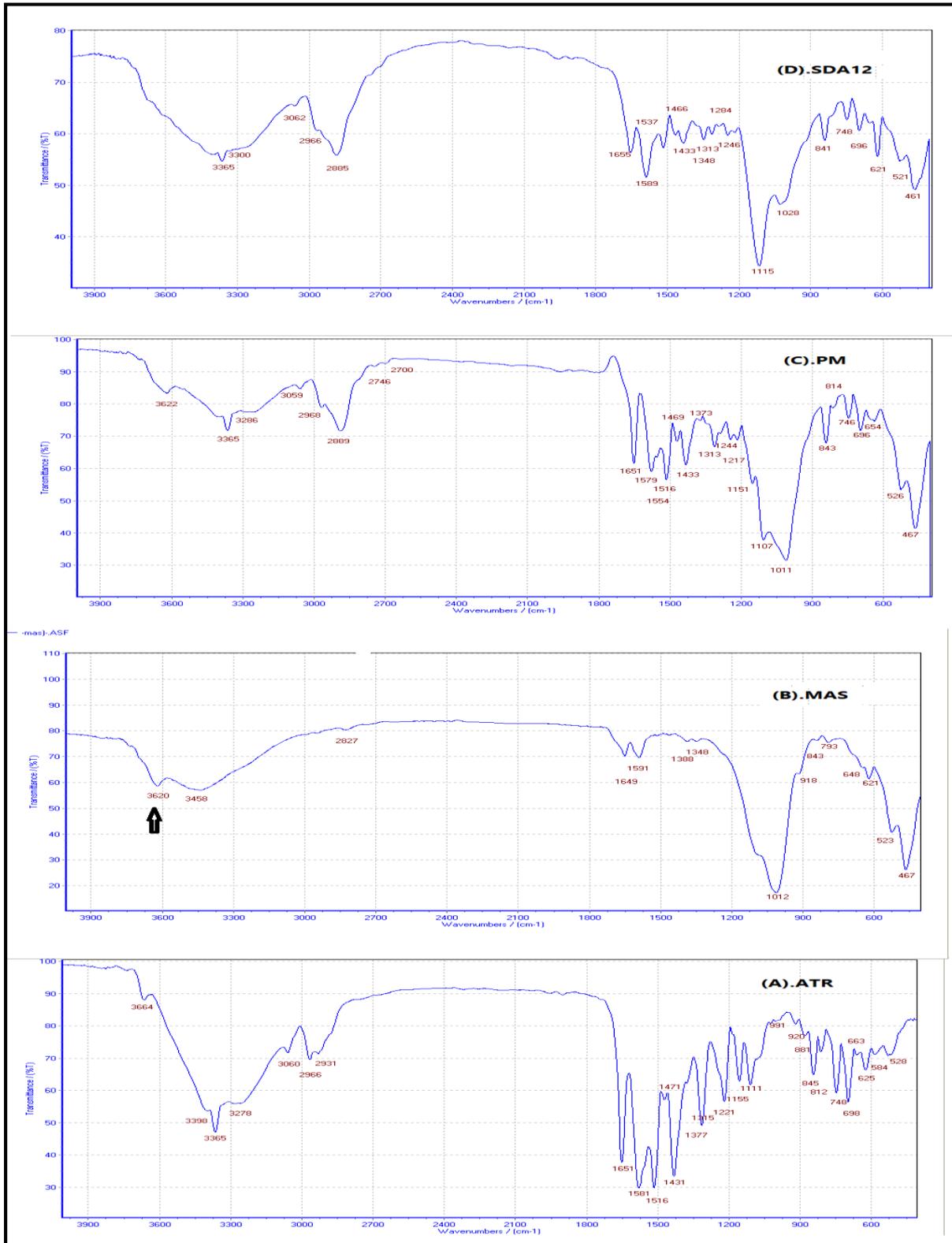


Figure 6. FTIR: ATR(A) , MAS (B) , PM (C) , SDA12 (D)

Conclusion

An improvement in solubility and dissolution of ATR was obtained by preparing it as solid dispersion adsorbate by melt adsorption method using hydrophilic carriers and adsorbents in a ratio of 1:1:1(drug: carrier: adsorbent).

All prepared formula of SDAs improved the solubility of ATR may be due to increased wettability and reduced crystallinity of the drug, which leads to improve drug solubility and dissolution.

However, Maximum solubility with enhanced dissolution was obtained by SDA12 using poloxamer 407 as a hydrophilic carrier with surfactant effect and MAS as an adsorbent with high surface area.

Acknowledgement

The authors are grateful to acknowledge the College of Pharmacy -University of Baghdad for providing the necessary facilities to carry out this study. The authors are also thankful to Pioneer Pharmaceutical Company, Iraq, for their generous help for providing gift sample of atorvastatin, Aerosil200 and PEG 6000.

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