IJPSR (2025), Volume 16, Issue 1 (Research Article)

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 28 July 2024; received in revised form, 23 October 2024; accepted, 26 December 2024; published 01 January 2025

QUALITY ASSESSMENT AND COMPARATIVE STUDY OF DIFFERENT MARKETED BRANDS OF SIMVASTATIN IN MALAYSIA

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Keywords:

Simvastatin, Characterization, Dissolution, Quality assessment, Pharmacopoeia

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ABSTRACT: Introduction: Simvastatin is one of the cholesterol-reducing agents, in the class of statins which is an HMG-CoA reductase inhibitors, used in the treatment of hyperlipidemia. It was categorized in biopharmaceutics classification system (BCS) class II drug, which has low solubility in aqueous media. It is a white-to-off white crystalline and non-hygroscopic powder, insoluble in water, but soluble in methanol, chloroform, and ethanol. Characterization test as FTIR spectroscopy was important to identify the identity of tablets. Tablets properties were evaluated by various physicochemical parameters including dissolution test to examine the equivalence and quality of different marketed brands of Simvastatin. They should comply with the specified pharmacopoeia limit for each test. **Objectives:** Objective of this study was to analyze the identity and evaluate the quality control parameters of different brands of Simvastatin with the specified pharmacopoeia limit. **Method:** Different brands of Simvastatin 20 mg tablets were collected by purchasing from local pharmacies in Malaysia. Physicochemical parameters such as weight variation, thickness and diameter measurement were performed. Besides, characterization test using FTIR spectrophotometer, dissolution test as well as disintegration test of each brand of Simvastatin tablets were also performed. **Results:** There were no abnormalities in the physical appearance of all tablets from different brands. All the brands complied with the official specifications for weight uniformity where no tablet showed deviation more than ±7.5%. Thickness, diameter measurement and disintegration test of each brand of Simvastatin tablets also passed the specified limit. Characterization test using FTIR spectrophotometer confirmed the identity of Simvastatin with peak of aromatic hydroxyl group around 3700-3100 cm-1, methyl group around 3000 -2800 cm-1 and aromatic carbonyl group around 1800 -1600 cm-1, except the standard Simvastatin showed strong and sharp peak for aromatic carbonyl group whereas other brands showed weak peak. A Characterization test using MS also confirmed the identity of Simvastatin with base peak of 419.3 m/z for protonated molecular ion [Simvastatin + H] + and major product ions at 199 m/z and 285 m/z were also observed compared to standard Simvastatin. Regarding dissolution test, Brand B achieved a bioavailability rate of 80.35%, AUC0-2 44.47 mg.hr/l and Brand E achieved a bioavailability rate of 70.11%, AUC0-2 29.8 mg.hr/l which was the highest among the brands tested, indicate immediate drug release pattern. Other brands might exhibit more sustained release profiles over a longer period of time. **Conclusion:** Results of all the parameters such as weight variation, thickness, diameter, and disintegration test obtained from the study comply with the USP and BP Pharmacopoeia limits. Brand C was identified having the most immediate drug release based on AUC despite the initial low percentage of release rate. Brands A and D showed prolonged drug release whereas Brand B and E showed potential immediate drug release.

INTRODUCTION: Hypercholesterolemia is one of the risk factors for cardiovascular disease (CVD), the leading cause of morbidity and mortality worldwide. Based on the 2015 Malaysian Ministry of Health report, the overall prevalence of hyper-cholesterolemia among Malaysian adults was 47.7% and 38.6% were undiagnosed [2].

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.16(1).241-57

This article can be accessed online on www.ijpsr.com

DOI link: https://doi.org/10.13040/IJPSR.0975-8232.16(1).241-57

Simvastatin is one of the cholesterol-reducing agents, in the class of statins. Statins in the group of 3-hydroxy-3- methyl-glutaryl coenzyme A (HMG-CoA) reductase inhibitors, were used in the treatment of hyperlipidemia as higher level of low-density lipoprotein (LDL) cholesterol can lead to artery damage, stroke and cardiac complications [37].

Based on the Malaysia statistics on drugs in 2015 and 2016, the use of Simvastatin in the public sector has markedly increased up to 65% in the 2015 and 2016 cohorts compared to the 2013 and 2014 cohorts. Simvastatin also remained within the top 10 drugs from 2015 to 2016 in the public sector [27]. That's why to carry out the study of "Quality Assessment and Comparative Study of Different Marketed Brands of Simvastatin Tablets in Malaysia". Simvastatin is a white-to-off white crystalline and non-hygroscopic powder which is insoluble in water, but soluble in methanol, chloroform, and ethanol. It is also an inactive prodrug, good oral absorption but undergoes hepatic first-pass metabolism, resulting in low bioavailability [29], which in turn shows rate-limited oral absorption and differences in pharmacological effects. Biotransformation takes place in the liver by ring- opening reaction of the lactone [17], convert to active form of Simvastatin (β- hydroxy acid) because the simvastatin lactone form favors hydrolysis due to unstable at higher pH values, opening the lactone and yielding the hydroxyl acid form as shown in **Fig. 1** [29]. It helps lower cholesterol production by preventing HMG-CoA production, causes decrease in low-density lipoprotein (LDL) (20 – 40 %) and triglycerides (10 – 20 %), while increases the high-density lipoprotein (HDL) (5– 15 %) [17].

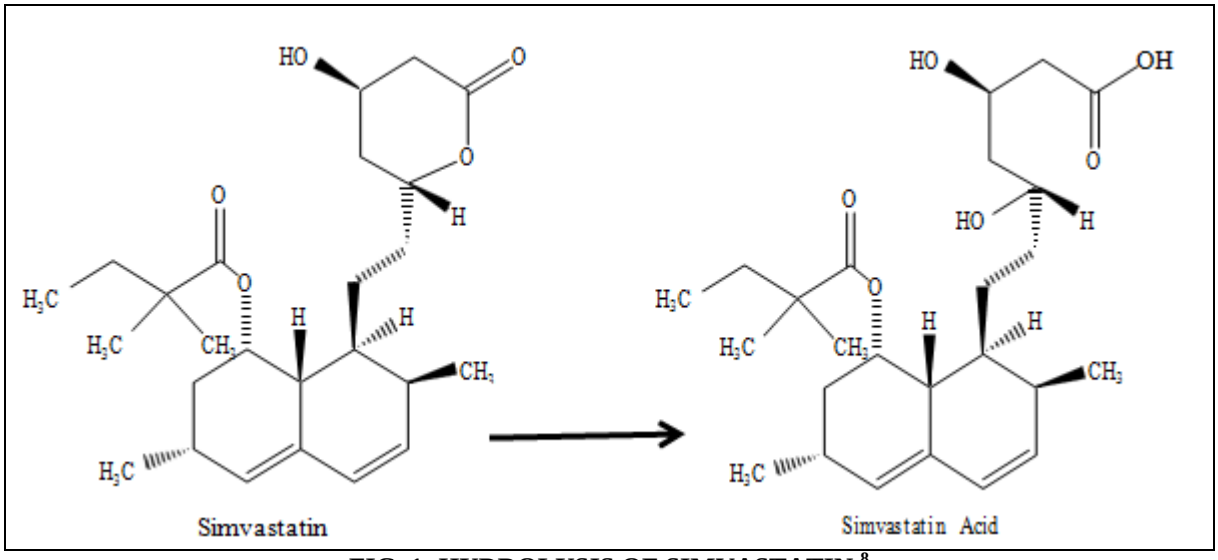


FIG. 1: HYDROLYSIS OF SIMVASTATIN [8]

Characterization of the tablets using Differential Scanning Calorimetry (DSC), Fourier- Transform Infrared Spectroscopy (FTIR) and Mass Spectrometry (MS) were important to identify the identity of tablets whereas the tablets properties usually evaluated through various physicochemical parameters. FTIR spectroscopy is a powerful characterization technique with high chemical specificity, that provides information on molecular structure based on the absorption of infrared light (IR) [19]. Attenuated total reflection (ATR) mode is the most suitable as sample thickness was not a limiting factor thus ATR- FTIR is used to analyze range of sample forms with minimal sample preparation. Nowadays, the widespread availability of multiple brands of Simvastatin tablets in Malaysia has prompted a growing concern among healthcare professionals about the challenges associated with generic brand substitution. It becomes imperative to assess the physicochemical equivalence of these formulations to make informed decisions regarding interchangeability [38]. It was important to examine the equivalence and quality of different marketed drug brands, especially used to manage chronic conditions such as hyperlipidemia. Healthcare systems encourage the replacement of originator with generic products due to the same quality and low cost, thus, the quality of these generic products was required to evaluate consistently. Quality assurance of pharmaceutical products influences quality; thus, the dissolution tests are very essential to evaluate different brands available to ensure performance and quality of finished products. It was also important to ensure efficacious and safety of products for patients at an affordable cost. For

example, like Simvastatin, some unpredictable dissolution profile outcomes might be possible as it was an inactive pro-drug and practically insoluble in water [14]. Dissolution was defined as the amount of substance released into solution per unit time under standardized conditions such as temperature and composition of solvent. Although dissolution cannot be used as a predictor of therapeutic efficiency, it can be used as quantitative and qualitative tool, which provides useful information about the drug's biological availability [4].

Objectives: The objectives of this study are to identify the physicochemical parameters such as weight variation, thickness and diameter, as well as compare the disintegration and dissolution of different brands of Simvastatin with the specified limit. We also want to identify and analyze the identity of different brands of Simvastatin tablets based on the spectrum obtained from spectrometers. Dissolution of drugs being the important parameters to evaluate the quality and efficacy of a drug thus, to determine and compare the percentage drug release in dissolution with different brands of Simvastatin. During the research, there was a need to understand and consistently follow the USP guidelines to prevent errors from occurring during handling of the experiment.

Methodology Sample Collection: Simvastatin 20 mg tablets produced by different pharmaceutical companies were collected by purchasing from local pharmacies in Malaysia. The study was performed within tablet expiration dates.

Physicochemical Parameters:
Materials: Simvastatin 20mg tablets **(**Brand A, B, C, D and E).

Equipment: Digital weighing balance**,** digital vernier caliper.

Weight Variation Test: 20 tablets of each brand of simvastatin tablets were weighed individually using digital weighing balance and got the average value for each brand.

Diameter and Thickness Measurement: The diameter and thickness of 20 tablets of each brand of simvastatin tablets were measured by using digital vernier caliper and get average diameter and thickness for each brand. Diameter deviation was then calculated using formula below [31].

Characterization test using FTIR spectrophotometer:
Materials: Standard Simvastatin 20mg powder (98%) (Thermo Scientific), Simvastatin 20mg tablets (Brand A, B, C, D and E), isopropyl alcohol.

Equipment: PerkinElmer Fourier Transform Infrared Spectroscopy (FTIR)

Dissolution Test:
Materials: Standard Simvastatin 20mg powder (98%) (Thermo Scientific), Simvastatin 20mg tablets (Brand A, B, C, D and E), sodium dodecyl sulfate (SDS), monobasic sodium phosphate, distilled water, sodium hydroxide.

Equipment: Shimadzu UV-1800 spectro-photometer, Pharma test USP apparatus II (Rotating Paddle apparatus), pH meter, volumetric flask, cuvette.

Preparation of Dissolution Medium: pH 7.0 buffer solution containing 0.5% sodium dodecyl sulfate (SDS) in 0.01M sodium phosphate prepared by dissolving 30 g of SDS and 8.28 g of monobasic sodium phosphate in 6000 mL of water and adjusting with 50% (w/v) sodium hydroxide solution to a pH of 7.0 and 900 mL (United State Pharmacopeia, 2005).

Preparation of Blank Solution: 10ml of pH 7.0 buffer solution was diluted to 50ml in volumetric flask, used as blank sample.

Preparation of Standard Simvastatin Solution: 5mg of reference Simvastatin was accurately weight, dissolve in 10ml of phosphate buffer solution pH 7.0 then transfer to 50ml volumetric flask, make up the volume by distilled water. This solution had a concentration of 100µg/ml (stock solution). Label as solution A. From solution a, five different serial solutions were prepared with the following concentration (10 µg/ml, 20 µg/ml, 30 µg/ml, 40 µg/ml and 50 µg/ml). To prepare each dilution, pipette out required volume (1ml, 2ml, 3ml, 4ml and 5ml respectively) into 10 ml volumetric flask and make up to volume with distilled water, then observed the absorbance under UV-Visible spectro-photometer with 1cm path-

length quartz cell at wavelength of 238nm, used distilled water as blank reading.

Sample Analysis: Dissolution test of each Simvastatin brand (Brand A, B, C, D and E) was performed using USP apparatus-II (Paddle) at 37 ±0.5 °C in 900 ml phosphate buffer medium with 0.5% SDS at pH 7.0 and 50 rpm [28]. Six tablets of brand A were placed into each vessel. 10 ml sample was withdrawn from the dissolution medium at 30- 60- 90 and 120- minutes interval, followed by immediate replacement of fresh dissolution medium for the acquisition of sink condition. Each sample was then filtered through Whatman filter No. 41 [5]. The 10 ml solutions were then diluted to 50 ml and assayed under UV-Visible spectrophotometer with 1cm path-length quartz cell at 238nm to determine the absorbance of each tablet for each brand of Simvastatin released in the dissolution test. The dissolution experiments were repeated for brand B, C, D and E respectively. Insert the absorbance of sample solution into the standard equation to calculate the concentration of each six tablets for each brand. Then calculate the drug release amount and percentage of drug release using formula below, get the average percentage drug release for each brand then plot graph of average percentage of drug release (%) against time (minutes).

Disintegration Test:
Materials: Simvastatin 20 mg tablets (Brand A, B, C, D and E), distilled water.

Equipment: Disintegration test apparatus
Procedure: Four tablets of Brand A were placed in each vessel along with plastic disk over each tablet and the apparatus (basket-rack assembly) was operated using distilled water at 37°C. Tubes were allowed to move up and down.

After 30 minutes, stop the disintegration apparatus and observe if each tablet had disintegrated completely and pass through the screen. The plastic disks do not allow the tablets to float and imparts slight pressure on the tablets to force any soft mass through screen. The procedures were repeated for Brand B, C, D and E. While the Appearance and descriptions of five different brands of Simvastatin 20mg tablets is shown in **Tables 1** and **2.**

Label Information:

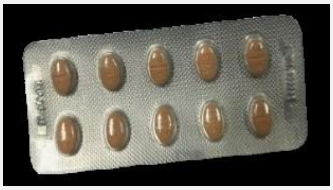
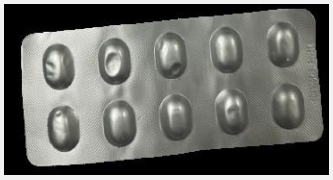
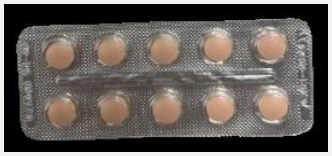
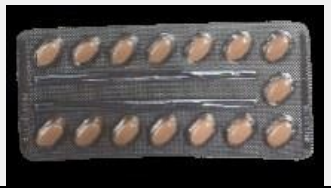
TABLE 1: LABEL INFORMATION OF FIVE DIFFERENT BRANDS OF SIMVASTATIN 20MG TABLETS

Brands	Expire date	Ingredients
A	03/2026	Simvastatin, Microcrystalline cellulose, Pregelatinised starch, Magnesium stearate, Purified water, Butylated hydroxyanisole, Isopropyl alcohol, Low substitutedhydroxypropyl cellulose, Opadry yellow, Opadry brown, Opadry pink, Lactose.
B	05/2025	Simvastatin, Microcrystalline cellulose, Starch, Magnesium stearate, Butylated hydroxyl lanisole, Ascorbic acid, Citric acid anhydrous, Opadry orange, Lactose monohydrate.
C	01/2027	Simvastatin, Microcrystalline cellulose, Starch, Magnesium stearate, Butylated hydroxytoluene, Ascorbic acid, Citric acid anhydrous, Ethanol, Opadry pink, Lactosemonohydrate.
D	01/2025	Simvastatin, Microcrystalline cellulose, Pregelatinised starch, Magnesium stearate, Purified water, Butylated hydroxyanisole, Hydroxypropyl cellulose, Hydroxypropyl methylcellulose, Ascorbic acid, Citric acid monohydrate, Lactose monohydrate, talc, titanium dioxide, iron oxide.
E	06/2025	Simvastatin, Cellulose, Pregelatinised starch, Magnesium stearate, Butylated hydroxyanisole, Ascorbic acid, Citric acid monohydrate, Lactose monohydrate, Hypromellose, Hyprolose.,

Appearance and Descriptions:

TABLE 2: APPEARANCE AND DESCRIPTIONS OF FIVE DIFFERENT BRANDS OF SIMVASTATIN 20MG TABLETS

Brands	Shape	Colour	Convexity	Descriptions
A 	Oval	Nude pink	Film-coated	One strip contains 10 tablets

B 	Oblong	Nude orange	Film-coated	One strip contains 10 tablets
C 	Oblong	Nude orange	Film-coated	One strip contains 10tablets
D 	Round	Orange	Film-coated	One strip contains 10 tablets
E 	Oval	Pink	Film-coated	One strip contains 15tablets

Physicochemical Parameters: Average weight of different brands of Simvastatin tablets.

TABLE 3: AVERAGE WEIGHT OF FIVE DIFFERENT BRANDS OF SIMVASTATIN 20MG TABLETS

Tablets	Weight (mg)				
	Brand A	Brand B	Brand C	Brand D	Brand E
Averageweight	205.87	205.22	207.92	207.98	207.20

From **Table 3,** the average weight of brand A, B, C, D and E was 205.87 mg, 205.22 mg, 207.92mg, 207.98 mg and 207.20 mg respectively. Brand D had the highest weight while brand B had lowest weight. While the average weight of 20 tablets of five different brands of Simvastatin 20 mg tablets is shown in **Fig. 1.** Since, the average weight of all different brands of Simvastatin tablets were within the 80 mg to 250 mg, thus minimum 18 tablets should not deviate from average weight by ±7.5% based on BP [10]. From **Table 3**, the highest deviation from brand A, B, C, D and E does not exceed ±7.5%, thus it passed the test. Average weight of five different brands of simvastatin is shown in **Fig. 2.**

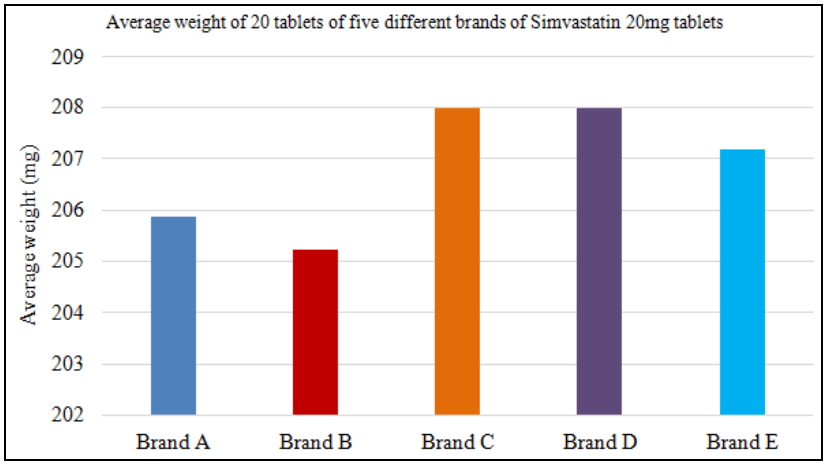


FIG. 2: AVERAGE WEIGHT OF FIVE DIFFERENT BRANDS OF SIMVASTATIN

Thickness of Different Brands of Simvastatin Tablets:

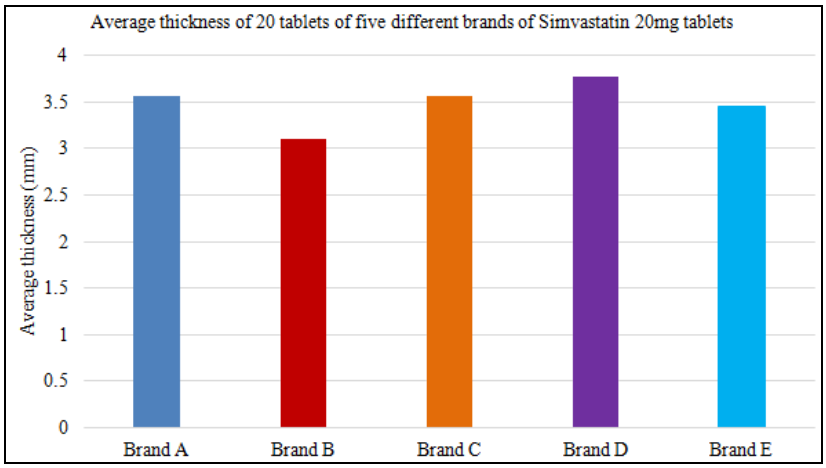


FIG. 3: AVERAGE THICKNESS OF FIVE DIFFERENT BRANDS OF SIMVASTATIN

Diameter of Different Brands of Simvastatin Tablets: Average diameter of each brand of Simvastatin tablets was shown in **Fig. 3.** The average diameter of brand A, B, C, D and E was 10.13 mm, 11.12 mm, 11.09 mm, 8.09 mm, and 11.17 mm respectively. Brand D has a shorter diameter (8.09 mm) while brand E has a larger diameter (11.17 mm). Thickness and diameter of 20 tablets of five different brands of Simvastatin is shown in **Fig. 3** and **4**, respectively.

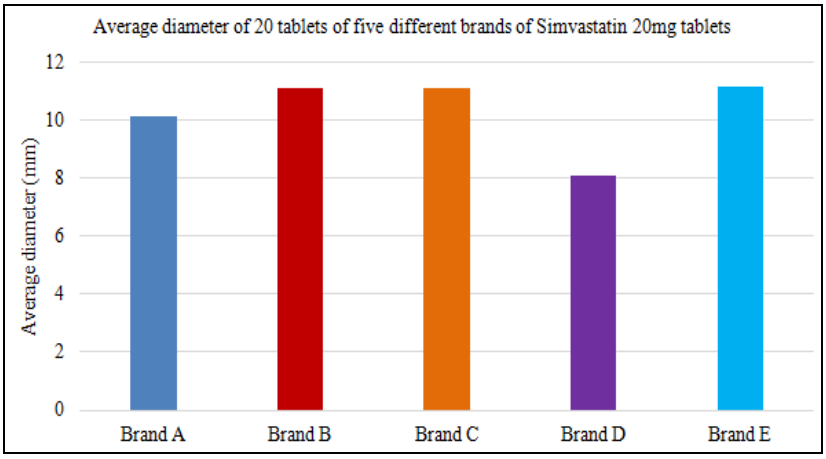


FIG. 4: AVERAGE DIAMETER OF 20 TABLETS OF FIVE DIFFERENT BRANDS OF SIMVASTATIN

Characterization Test FTIR Spectrophotometer: FTIR spectrum of standard Simvastatin is laid down in **Fig. 5.**

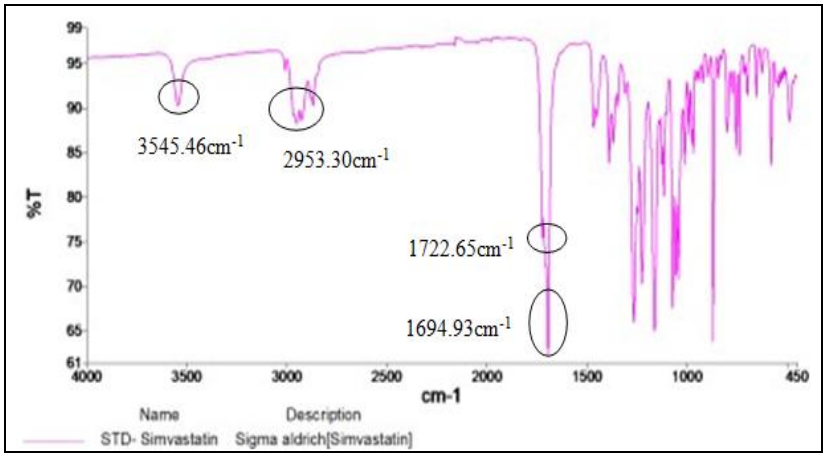


FIG. 5: FTIR SPECTRUM OF STANDARD SIMVASTATIN

TABLE 4: FTIR SPECTRUM OF STANDARD SIMVASTATIN

Peak number	Wave number (cm $^{-1}$)	Functional groups	Type of vibration	Type of peak
1	3545.46	Aromatic hydroxyl group (O-H)	Stretching	Broad peak
2	2953.30	Alkane group (C-H)	Stretching	-
4	1722.65	Aromatic Carbonyl group (C=O)	Stretching	Sharp and strong peak
5	1694.93	Aromatic Carbonyl group (C=O)	Stretching	Sharp and strong peak

FTIR spectrum of Standard Simvastatin is shown in **Fig. 3** and **Table 4**, respectively. Stretching vibration of carbonyl group (C=O) in peak number 4 and 5 were for ester and lactone. For the Brand A, B, C, D and E, the spectra are given in **Fig. 6-10** respectively.

FTIR Spectrum of Brand A:

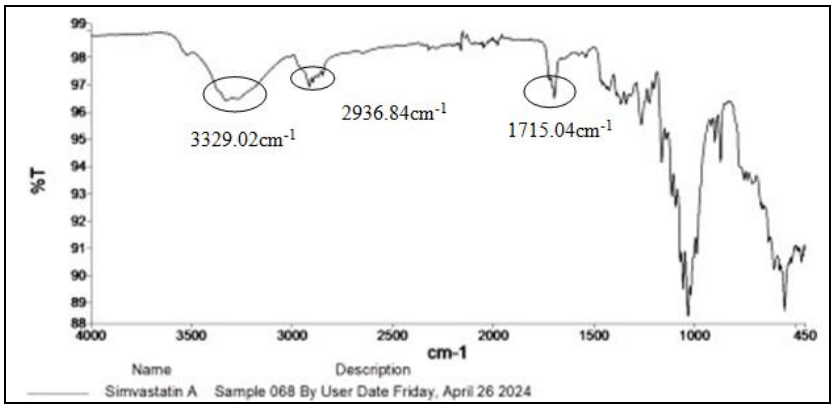


FIG. 6: FTIR SPECTRUM OF BRAND A

FTIR Spectrum of Brand B:

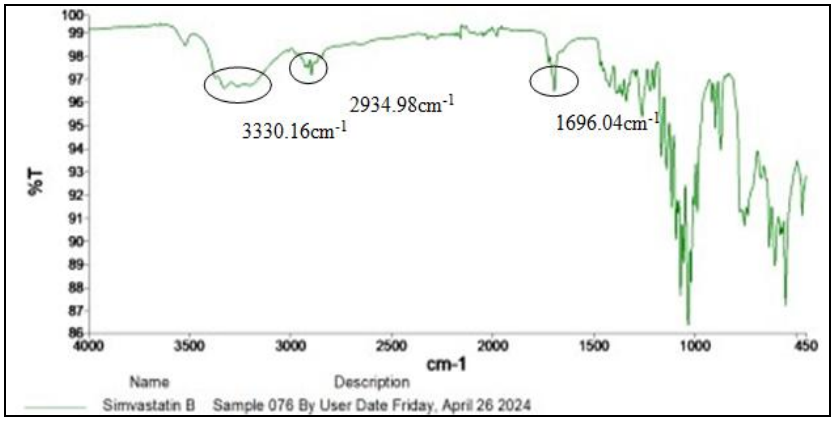


FIG. 7: FTIR SPECTRUM OF BRAND B.

FTIR Spectrum of Brand C:

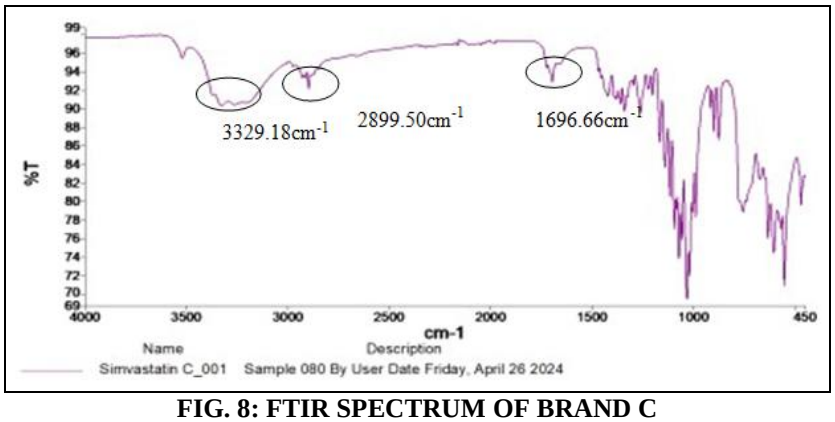


FIG. 8: FTIR SPECTRUM OF BRAND C

FTIR Spectrum of Brand D:

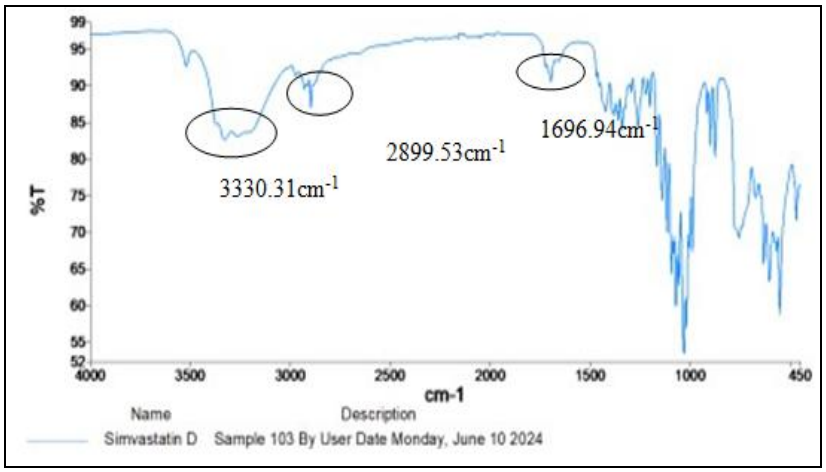


FIG. 9: FTIR SPECTRUM OF BRAND D

FTIR Spectrum of Brand E:

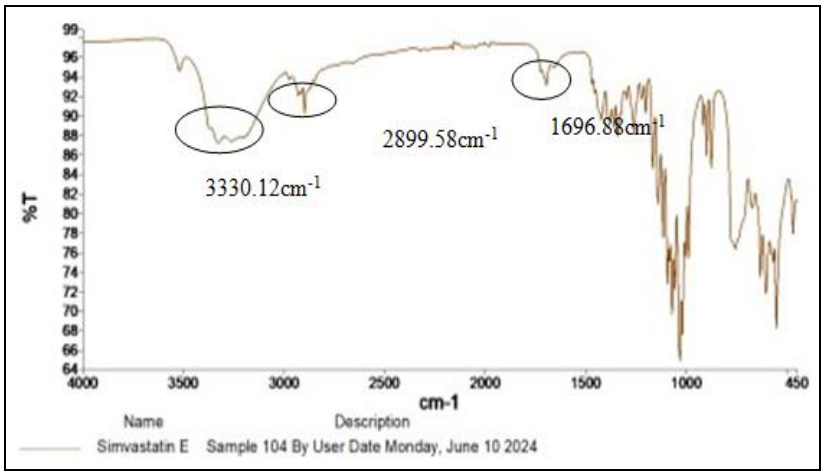


FIG. 10: FTIR SPECTRUM OF BRAND E

FTIR Spectrum of Different Brands of Simvastatin Tablets are shown in Fig. 9:

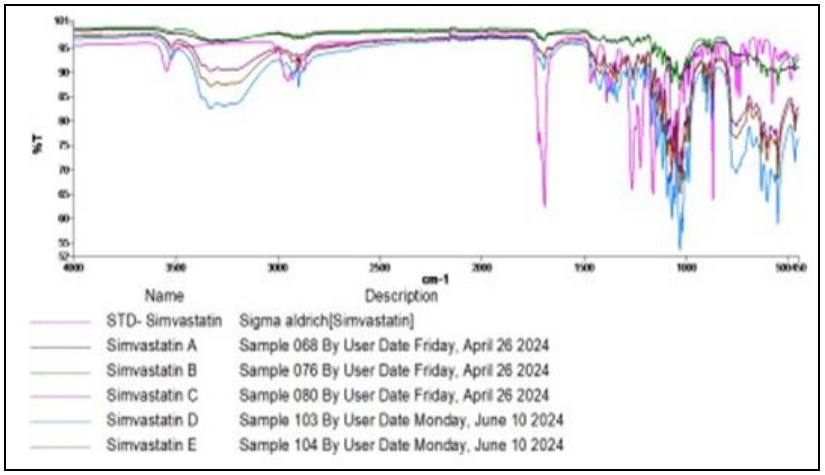


FIG. 11: FTIR SPECTRUM OF DIFFERENT BRANDS OF SIMVASTATIN TABLETS

All the different brands of Simvastatin (Brand A, B, C, D and E) shown in the **Fig. 11** had the same peak as per standard Simvastatin such as Aromatic hydroxyl group (O-H) around 3700cm^{-1} - 3100cm^{-1}, alkane group (C-H) around 3000cm^{-1} – 2800cm^{-1} and aromatic carbonyl group (C=O) around

1800cm^{-1}-1600cm^{-1}. The only different between standard Simvastatin and other brands of Simvastatin was the aromatic carbonyl group (C=O) with stretching vibration around wavelength 1800 -1600 cm $^{-1}$ showed sharp and strong peak in standard Simvastatin but weak peak in all other brands of Simvastatin (Brand A, B, C, D and E).

Mass Spectrometry:

Mass Spectrum of Standard Simvastatin:

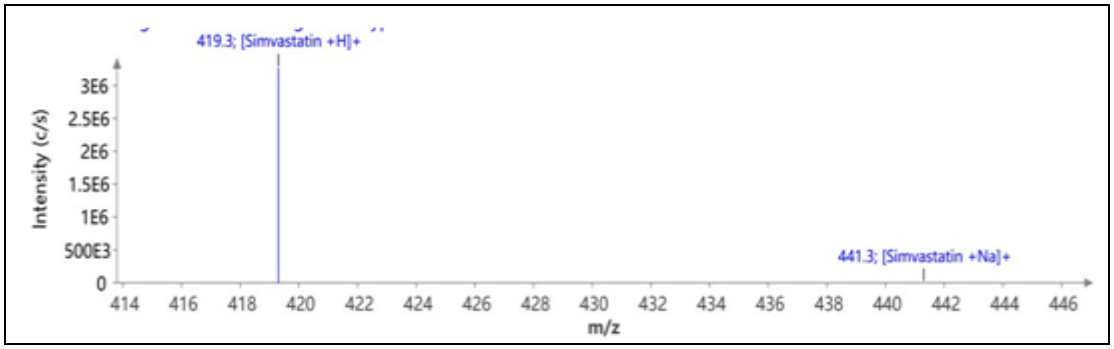


FIG. 12: MASS SPECTRUM OF STANDARD SIMVASTATIN OF PROTONATED PRODUCT ION (BASE PEAK)

Based on the results of analysis as shown in **Fig. 12**, it is confirmed that the appearance of simvastatin in this standard Simvastatin with identified peak (base peak) of 419.3 m/z for protonated molecular ion [Simvastatin + H] $^{+}$. Major product ions at 199 m/z and 285 m/z were also observed.

Mass Spectrum of Brand A:

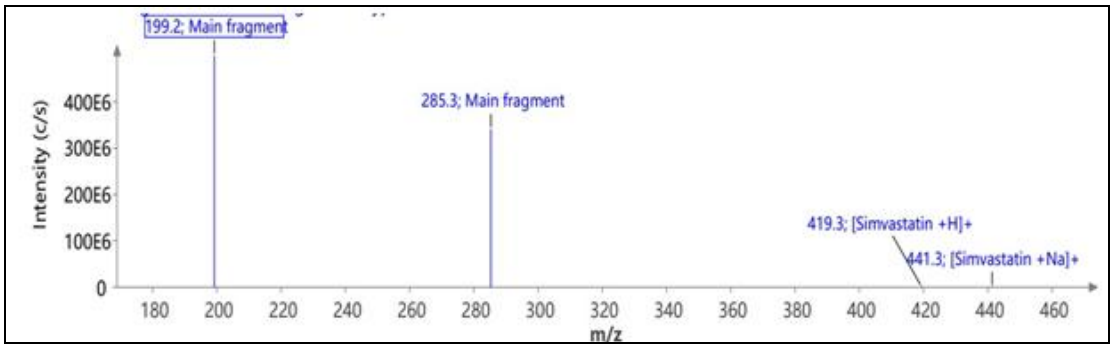


FIG. 13: MASS SPECTRUM OF BRAND A OF SIMVASTATIN PRODUCT ION AND PROTONATED MOLECULAR ION (BASE PEAK)

Based on the results of analysis as shown in **Fig. 13,** it is confirmed that the appearance of simvastatin in Brand A as the peak of 419.3 m/z for protonated molecular ion (base peak) and major product ions at 199 m/z and 285 m/z were also observed.

Mass Spectrum of Brand B:

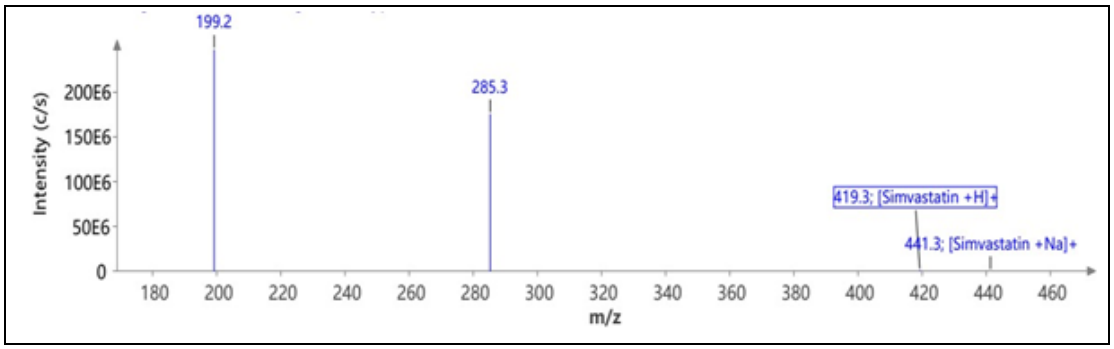


FIG. 14: MASS SPECTRUM OF BRAND B OF SIMVASTATIN PRODUCT ION AND PROTONATE MOLECULAR ION (BASE PEAK)

Based on the results of analysis as shown in **Fig. 14** and compare with the reference standard in **Fig. 4**, it is confirmed that the appearance of simvastatin in Brand B as the peak of 419.3 m/z for protonated molecular ion (base peak) and major product ions at 199 m/z and 285 m/z were also observed.

Mass Spectrum of Brand C:

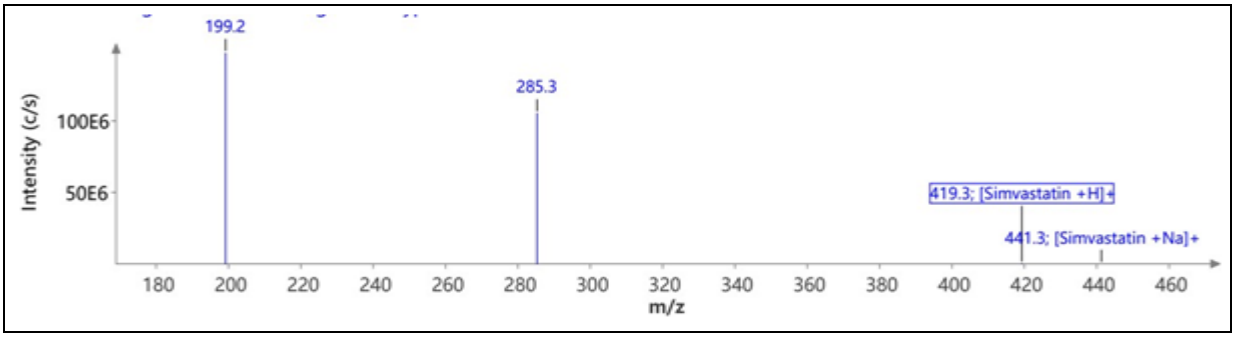


FIG. 15: MASS SPECTRUM OF BRAND C OF SIMVASTATIN PRODUCT ION AND PROTONATED MOLECULAR ION (BASE PEAK)

Based on the results of analysis as shown in **Fig. 15** and compare with the reference standard in **Fig. 4**, it is confirmed that the appearance of simvastatin in Brand C as the peak of 419.3 m/z for protonated molecular ion (base peak) and major product ions at 199 m/z and 285 m/z were also observed.

Dissolution Test: The calibration curve of standard simvastatin is shown in **Fig. 16.**

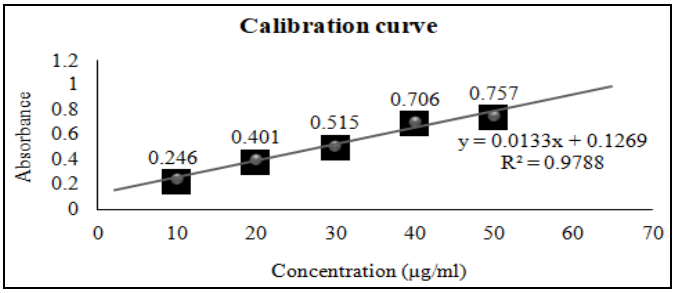


FIG. 16: CALIBRATION CURVE OF STANDARD SIMVASTATIN

Average Percentage Drug Release (%) of Brand A:

TABLE 5: AVERAGE PERCENTAGE DRUG RELEASE (%) OF BRAND A

Brands	Time (min)	Tablets	Average absorbance reading (y)	Concentration (µg/ml) (x)	Drug release (mg)	Percentage drug release (%)
Brand A	30 min	Tablet 1	0.167	3.015	2.714	6.784
		Tablet 2	0.224	7.301	6.571	16.427
		Tablet 3	0.207	6.023	5.420	13.551
		Tablet 4	0.196	5.195	4.676	11.690
		Tablet 5	0.266	10.459	9.413	23.532
		Tablet 6	0.196	5.195	4.676	11.690
	Average percentage drug release (%)					**13.946**
	60 min	Tablet 1	0.209	6.173	5.556	13.889
		Tablet 2	0.248	9.105	8.195	20.487
		Tablet 3	0.273	10.985	9.886	24.716
		Tablet 4	0.268	10.609	9.548	23.870
		Tablet 5	0.281	11.586	10.428	26.070
		Tablet 6	0.265	10.383	9.345	23.363
	Average percentage drug release (%)					**22.066**
	90 min	Tablet 1	0.216	6.699	6.029	15.073
		Tablet 2	0.256	9.707	8.736	21.840
		Tablet 3	0.269	10.684	9.616	24.039
		Tablet 4	0.278	11.361	10.225	25.562
		Tablet 5	0.283	11.737	10.563	26.408
		Tablet 6	0.269	10.684	9.616	24.039
	Average percentage drug release (%)					**22.827**

Based on **Table 5**, the average percentage drug release of Brand A for all six tablets in 30 min, 60 min, 90 min and 120 min were 13.95%, 22.07%, 22.83% and 24.10% respectively.

Average Percentage Drug Release (%) of Brand B:

TABLE 6: AVERAGE PERCENTAGE DRUG RELEASE (%) OF BRAND B

Brands	Time(min)	Tablets	Average absorbance reading (y)	Concentration (µg/ml) (x)	Drug release (mg)	Percentage drug release (%)
Brand B	30 min	Tablet 1	0.379	18.955	17.059	42.649
		Tablet 2	0.386	19.48	17.533	43.833
		Tablet 3	0.370	18.278	16.450	41.126
		Tablet 4	0.379	18.955	17.059	42.649
		Tablet 5	0.386	19.481	17.533	43.833
		Tablet 6	0.384	19.331	17.398	43.494
	Average percentage drug release (%)					**42.931**
	60 min	Tablet 1	0.386	19.481	17.533	43.833
		Tablet 2	0.392	19.932	17.939	44.848
		Tablet 3	0.397	20.308	18.277	45.694
		Tablet 4	0.387	19.556	17.601	44.002
		Tablet 5	**0.359**	17.451	15.706	39.265
		Tablet 6	**0.385**	19.406	17.465	43.664
	Average percentage drug release (%)					**43.551**
	90 min	Tablet 1	0.551	31.887	28.699	71.746
		Tablet 2	0.565	32.940	29.646	74.115
		Tablet 3	0.551	31.887	28.699	71.746
		Tablet 4	0.537	30.835	27.751	69.378
		Tablet 5	0.555	32.188	28.969	72.423
		Tablet 6	0.561	32.639	29.375	73.438
	Average percentage drug release (%)					**72.141**
	120 min	Tablet 1	0.620	37.075	33.368	83.419
		Tablet 2	0.601	35.647	32.082	80.205
		Tablet 3	0.602	35.722	32.150	80.374
		Tablet 4	0.642	38.729	34.856	87.141
		Tablet 5	0.541	31.135	28.022	70.055
		Tablet 6	0.605	35.947	32.353	80.882
	Average percentage drug release (%)					**80.346**

Based on **Table 6,** the average percentage drug release of Brand B for all six tablets in 30 min, 60 min, 90 min and 120 min were 42.93%, 43.55%, 72.14% and 80.35% respectively.

Average Percentage Drug Release (%) of Brand C:

TABLE 7: AVERAGE PERCENTAGE DRUG RELEASE (%) OF BRAND C

Brands	Time (min)	Tablets	Average absorbance reading (y)	Concentration (µg/ml) (x)	Drug release (mg)	Percentagedrug release (%)
Brand C	30 min	Tablet 1	0.285	11.887	10.699	26.746
		Tablet 2	0.289	12.188	10.969	27.423
		Tablet 3	0.291	12.338	11.105	27.761
		Tablet 4	0.303	13.241	11.917	29.791
		Tablet 5	0.294	12.564	11.308	28.269
		Tablet 6	0.292	12.414	11.172	27.930
	Average percentage drug release (%)					**27.987**
	60 min	Tablet 1	0.294	12.564	11.308	28.269
		Tablet 2	0.297	12.789	11.511	28.776
		Tablet 3	0.294	12.564	11.308	28.269
		Tablet 4	0.300	13.015	11.714	29.284
		Tablet 5	0.293	12.489	11.240	28.100
		Tablet 6	0.298	12.865	11.578	28.945
	Average percentage drug release (%)					**28.607**
	90 min	Tablet 1	0.304	13.316	11.984	29.961
		Tablet 2	0.303	13.241	11.917	29.791
		Tablet 3	0.299	12.940	11.646	29.115

		Tablet 4	0.360	17.526	15.774	39.434
		Tablet 5	0.304	13.316	11.984	29.961
		Tablet 6	0.300	13.015	11.714	29.284
		Average percentage drug release (%)				**31.258**
	120 min	Tablet 1	0.306	13.466	12.120	30.299
		Tablet 2	0.307	13.541	12.187	30.468
		Tablet 3	0.313	13.992	12.593	31.483
		Tablet 4	0.317	14.293	12.864	32.160
		Tablet 5	0.307	13.541	12.187	30.468
		Tablet 6	0.306	13.466	12.120	30.299
		Average percentage drug release (%)				**30.863**

Based on **Table 7,** the average percentage drug release of Brand C for all six tablets in 30 min, 60 min, 90 min and 120 min were 27.99%, 28.61%, 31.26% and 30.86% respectively.

Average Percentage Drug Release (%) of Brand D:

TABLE 8: AVERAGE PERCENTAGE DRUG RELEASE (%) OF BRAND D

Brands	Time (min)	Tablets	Average absorbance reading (y)	Concentration (µg/ml) (x)	Drug release(mg)	Percentagedrug release (%)
Brand D	30 min	Tablet 1	0.268	10.609	9.548	23.870
		Tablet 2	0.276	11.211	10.089	25.224
		Tablet 3	0.276	11.211	10.089	25.224
		Tablet 4	0.259	9.932	8.939	22.348
		Tablet 5	0.259	9.932	8.939	22.348
		Tablet 6	0.274	11.060	9.954	24.885
		Average percentage drug release (%)				**23.983**
	60 min	Tablet 1	0.227	7.556	6.801	17.002
		Tablet 2	0.280	11.511	10.360	25.900
		Tablet 3	0.278	11.361	10.225	25.562
		Tablet 4	0.283	11.737	10.563	26.408
		Tablet 5	0.272	10.910	9.819	24.547
		Tablet 6	0.281	11.586	10.428	26.070
		Average percentage drug release (%)				**24.248**
	90 min	Tablet 1	0.259	9.932	8.939	22.348
		Tablet 2	0.278	11.361	10.225	25.562
		Tablet 3	0.277	11.286	10.157	25.393
		Tablet 4	0.270	10.760	9.683	24.209
		Tablet 5	0.269	10.684	9.616	24.039
		Tablet 6	0.281	11.586	10.428	26.070
		Average percentage drug release (%)				**24.604**
	120 min	Tablet 1	0.278	11.361	10.225	25.562
		Tablet 2	0.285	11.887	10.699	26.746
		Tablet 3	0.285	11.887	10.699	26.746
		Tablet 4	0.285	11.887	10.699	26.746
		Tablet 5	0.277	11.286	10.157	25.393
		Tablet 6	0.290	12.263	11.037	27.59211
		Average percentage drug release (%)				**26.464**

Based on **Table 8,** the average percentage drug release of Brand D for all six tablets in 30 min, 60 min, 90 min and 120 min were 23.98%, 24.25%, 24.60% and 26.46% respectively.

Average Percentage Drug Release (%) of Brand E:

TABLE 9: AVERAGE PERCENTAGE DRUG RELEASE (%) OF BRAND E

Brands	Time (min)	Tablets	Average absorbance reading (y)	Concentration (µg/ml) (x)	Drug release (mg)	Percentagedrug release (%)
		Tablet 1	0.282	11.662	10.495	26.239
		Tablet 2	0.273	10.985	9.886	24.716

Brand E	30 min	Tablet 3	0.283	11.737	10.563	26.408
		Tablet 4	0.274	11.060	9.954	24.885
		Tablet 5	0.285	11.887	10.699	26.746
		Tablet 6	0.283	11.737	10.563	26.408
		Average percentage drug release (%)				**25.900**
	60 min	Tablet 1	0.345	16.399	14.759	36.897
		Tablet 2	0.288	12.113	10.902	27.254
		Tablet 3	0.292	12.414	11.172	27.930
		Tablet 4	0.296	12.714	11.443	28.607
		Tablet 5	0.301	13.090	11.781	29.453
		Tablet 6	0.290	12.263	11.037	27.592
		Average percentage drug release (%)				**29.622**
	90 min	Tablet 1	0.501	28.128	25.315	63.288
		Tablet 2	0.350	16.774	15.097	37.742
		Tablet 3	0.340	16.023	14.420	36.051
		Tablet 4	0.338	15.872	14.285	35.712
		Tablet 5	0.331	15.346	13.811	34.528
		Tablet 6	0.424	22.338	20.105	50.261
		Average percentage drug release (%)				**42.930**
	120 min	Tablet 1	0.580	34.068	30.661	76.652
		Tablet 2	0.540	31.060	27.954	69.885
		Tablet 3	0.632	37.977	34.180	85.449
		Tablet 4	0.544	31.361	28.225	70.562
		Tablet 5	0.515	29.180	26.262	65.656
		Tablet 6	**0.437**	23.316	20.984	52.461
		Average percentage drug release (%)				**70.111**

Based on **Table 9,** the average percentage drug release of Brand E for all six tablets in 30 min, 60 min, 90 min and 120 min were 25.90%, 29.62%, 42.93% and 70.11% respectively.

Drug Release Profile of Different Brands of Simvastatin Tablets: Average percentage drug release (%) of all different brands of Simvastatin tablets is given in **Table 10.**

TABLE 10: AVERAGE PERCENTAGE DRUG RELEASE (%) OF ALL DIFFERENT BRANDS OF SIMVASTATIN TABLETS

Time (min)	Average percentage drug release (%)				
	Brand A	**Brand B**	**Brand C**	**Brand D**	**Brand E**
0 min	0	0	0	0	0
30 min	13.95	42.93	27.99	23.98	25.90
60 min	22.07	43.55	28.61	24.25	29.62
90 min	22.83	72.14	31.26	24.60	42.93
120 min	24.10	80.35	30.86	26.46	70.11

Drug release pattern of different brands of Simvastatin tablets is shown in **Fig. 17.**

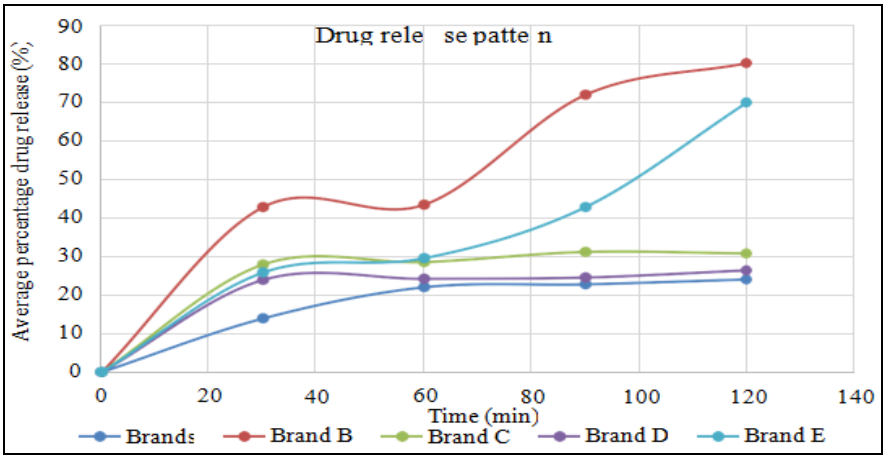


FIG. 17: DRUG RELEASE PATTERN OF DIFFERENT BRANDS OF SIMVASTATIN TABLETS

Based on **Fig. 16**, Brand B had highest percentage of drug release (80.35%) in 120 minutes while Brand A had lowest percentage of drug release (24.10%) at the same time. Brand A (24.10%), Brand C (30.86%), Brand D (26.46%) and Brand E (70.11%) released the drug at slower rate within the time intervals of 120 minutes. Area under curve $_{0-2}$ (AUC_{0-2}), C_{max} and T_{max} of different brands of Simvastatin tablets is given in **Table 11.**

TABLE 11: AREA UNDER CURVE $_{0-2}$ (AUC_{0-2}), C_{MAX} AND T_{MAX} OF DIFFERENT BRANDS OF SIMVASTATIN TABLETS

Brands	AUC_{0-2} (mg.hr/l)	C_{max} (mg/l)	T_{max} (hours)
Brand A	15.76	10.71	2 hours
Brand B	44.47	35.71	2 hours
Brand C	22.96	13.89	1.5 hours
Brand D	19.13	11.76	2 hours
Brand E	29.80	31.16	2 hours

Disintegration Test: Each different brand of Simvastatin tablets (Brand A, B, C, D, and E) passed the disintegration test, in which they successfully disintegrated within 30 minutes.

DISCUSSION: This research was conducted for quality assessment and compared different brands of Simvastatin tablets in Malaysia. Five different brands of Simvastatin tablets (Brand A, B, C, D and E) were obtained from local pharmacies in Malaysia and subjected to variety of tests in order to assess their quality control parameters. All investigated brands were within their shelf life during the tests. The assessments involved the evaluation of physical appearance, weight uniformity, thickness, diameter, characterization, disintegration and dissolution test. Both the United State Pharmacopoeia (USP) and British Pharmacopoeia (BP) act as the standard references for these studies. Weight variation test was one of the methods to determine content uniformity of tablets which should maintained by the manufacturers. In the experiment, since the average weight of Brand A, B, C, D and E obtained for 20 tablets was 205.87 mg, 205.22 mg,

207.92 mg, 207.98 mg and 207.20 mg respectively, which is within 80 to 250mg, thus minimum 18 tablets should not deviate from average weight by ±7.5% according to the BP [10]. The weight uniformity of tablets in brand A, B, C, D and E were acceptable as all 20 tablets do not deviate from ±7.5%, shown in Table 4. Since brand D had the highest weight (207.98 mg) while brand B had lowest weight (205.22 mg), brand D may contain more excipients and brand B may contain less excipients such as diluents, lubricant and so on. In short, all different brands of the Simvastatin tablets had almost uniform weight. Based on the result as shown in **Fig. 3**, the average thickness of 20 tablets in Brand A, B, C, D and E were 3.56 mm, 3.11 mm, 3.57 mm, 3.78 mm, and 3.45 mm respectively. The results showed a small difference in value which indicates the tablets had uniform thickness regardless of different brands.

In terms of the diameter of tablets, the average deviation of individual tablet should not exceed ± 5% for tablets with diameter less than 12.5 mm [8]. From the results as shown in Figure 4, the average diameter obtained for 20 tablets in Brand A, B, C, D and E were 10.13 mm, 11.12 mm, 11.09 mm, 8.09 mm, and 11.17 mm respectively. The highest deviation does not exceed 5%. Thus, the result showed the manufacturer complied with the pharmacopoeia standard. Diameter uniformity of tablets was very important to increase the patient compliance and avoid them from being confused with different size of the tablets because different size of the tablets may cause the patient to think that the drugs or tablets have different amount of active ingredient.

The characterization test was performed using FTIR and MS. FTIR spectrum divided into functional group region (4000 cm^{-1} – 1500 cm^{-1}) and fingerprint region (1500 cm^{-1}- 400 cm^{-1}). Here we only considered the functional group region. All the different brands of Simvastatin (Brand A, B, C, D, and E) have the same peak as per the spectrum of standard Simvastatin as shown in **Fig. 9**, such as aromatic hydroxyl group around 3700-3100 cm^{-1}, alkane group (C-H) around 3000 -2800 cm^{-1} and aromatic carbonyl group around 1800 -1600 cm^{-1} except the standard Simvastatin have strong and sharp peak for aromatic carbonyl group but other

brands of Simvastatin (Brand A, B, C, D and E) have only weak peak for aromatic carbonyl group. This may indicate the active pharmaceutical ingredient (API) present in other brands of Simvastatin was in lower concentration compared to standard Simvastatin. In short, these confirmed the identity of Simvastatin.

Additional test such as Mass Spectrophotometer was performed using the mass analysis by Compact Mass Spectrometer *via* Atmospheric Solids Analysis Probe (ASAP) to detect and confirm Simvastatin in various brands of Simvastatin from reference standard of Simvastatin. This test was performed for standard Simvastatin, Brand A, B and C as shown in Figures 6-10. All the Simvastatin brands performed confirmed the appearance of Simvastatin with identified peak (base peak) of 419.3 m/z for protonated molecular ion [Simvastatin + H] $^{+}$. Major product ions at 199 m/z and 285 m/z were also observed compared to standard Simvastatin. These confirmed the identity of Simvastatin.

The Dissolution test was an important quality control parameter related to drug absorption and bioavailability. It has a significant effect on their pharmacological activity. The percentage drug release of five brands of Simvastatin tablets were determined. In accordance with time intervals for drug release, all brands released the drug at specific time intervals after sample collection: 30 minutes, 60 minutes, 90 minutes, and 120 minutes (which totals of 2 hours).

Brand B achieved a bioavailability rate of 80.35% and Brand E achieved a bioavailability rate of 70.11%. AUC_{0-2} (Area under the curve from 0 to 2 hours) for Brand B was 44.47 mg.hr/l and for Brand E was 29.8 mg.hr/l. These values are the highest among the brands tested, indicating that these formulations release a significant amount of drug into systemic circulation within the first two hours after administration. This aligns with the high bioavailability rates observed for Brands B and E. The high AUC_{0-2} values confirm that Brands B and E exhibit potential immediate drug release characteristics during the study period. This immediate release profile correlates well with their high bioavailability rates, indicating efficient absorption and quick availability of the drug in the bloodstream. Comparatively, it suggests that other brands may show extended drug release profiles if the duration of the study were continued for a few more hours. This implies that while Brands B and E show immediate release characteristics, other brands might exhibit slower and more sustained release profiles over a longer period of time.

Various factors such as high level of humidity at storage area can increase the degradation rate of pharmaceutical drugs, make them softer and alter the dissolution profile. Besides, factors associated with dissolution test procedure may lead to variation or errors in the results such as the presence of air bubbles in the dissolution medium will cause problem in dissolution test and it should be avoided. If these bubbles adhered to the tablet, it would lead to a decreased exposed surface of tablet to direct contact with the media, decreased the dissolution rate, thus degassing the medium can help to minimize this issue. In addition, incompatibility between the active ingredient and excipients such as diluent (lactose) and binders (starch) can affect the stability and dissolution rate by delaying the drug release during the manufacturing process performed by pharmaceutical company. Moreover, different products may have been tested on the same equipment, thus it may cause the presence of impurities and failure of dissolution test if not cleaned well [3].

Disintegration test was the time recorded for a tablet to completely disintegrate, correlating to the drug's bioavailability. It was influenced by the rate of solvent influx into the tablets. The results showed that all the brands passed the disintegration test according to the pharmacopoeia which specifies 30 minutes for film coated tablets.

CONCLUSION: In conclusion, quality parameters of five marketed brands of Simvastatin 20 mg tablets were analysed by using various methods. The results of the parameters such as weight variation, thickness, diameter, and disintegration test obtained from the study comply with the USP and BP Pharmacopoeia limit. Brand B and E showed the highest rate of drug release compared to other brands within a two-hour duration after sample collection. As mentioned, Brand B and Brand E brands initially showed immediate drug

release patterns. However, there is a suggestion that they might exhibit delayed drug release if the dissolution study were extended by a few more hours. This indicates that their release profiles may change over time. Brands B and E showed the signs of potential immediate drug release. Although Brand C showed a relatively low percentage of drug release initially, its Area under the Curve (AUC) confirmed that it has the most immediate drug release formulation, particularly within 1.5 hours of the study. This suggests that Brand C releases the drug quickly despite the initial low percentage. Brand C is identified as having the most immediate drug release. Brand A and Brand D brands showed prolonged drug release profiles during the study. If more time were allowed for dissolution (beyond the current study duration), their percentage drug release and AUC would likely continue to increase, indicating a slower and more sustained release over time. Brands A and D exhibit prolonged drug release profiles that would likely continue to increase with more time in dissolution studies. It is mentioned that all brands would release the drug 100% if the study were completed over a duration of 12-16 hours. This suggests that the drug release was not instantaneous but occurs gradually over a longer period.

ACKNOWLEDGEMENT: Nil

CONFLICTS OF INTEREST: Nil

REFERENCES:

1. Abd Kadir Abu Bakar, Abdul Aiman Abd Ghani, Abu Bakar Rahman, Ahmad Ali Zainuddin, Ahmad Nadzri Jai and Arunah Chandran: National Health and Morbidity Survey 2015 Non- Communicable Diseases, Risk Factors &Other Health Problems. Institute for Public Health, National Institutes of Health, Ministry of Health 2015; (2): 13-23.
2. Abdul Murad NA, Mohammad Noor Y, Mohd. Rani Z, Sulaiman SA, Chow YP, Abdullah N, Ahmad N, Ismail N, Abdul Jalal N, Kamaruddin MA, Saperi AA & Jamal R: Hypercholesterolemia in the Malaysian CohortParticipants: Genetic and Non- Genetic Risk Factors. Genes 2023; 14(3): 721. https://doi.org/10.3390/genes14030721
3. Abend A, Curran D, Kuiper J, Lu X, Li H, Hermans A, Kotwal P, Diaz DA and Cohen MJ, Zhang L, Stippler E, Drazer G, Lin Y, Raines K, Yu L, Coutant CA, Grady H, Krämer J, Pope-Miksinski S & Suarez-Sharp S: Dissolution Testing in Drug Product Development: Workshop Summary Report. The AAPS Journal 2019; 21(2). https://doi.org/10.1208/s12248-018-0288-4.
4. Al Ameri MN, Nayuni N, Anil Kumar KG, Perrett D, Tucker A & Johnston A: The differences between the branded and generic medicines using solid dosage forms: *In-vitro* dissolution testing. Results in Pharma Sciences 2011; 2(2): 1–8. https://doi.org/10.1016/j.rinphs.2011.12.001
5. Kim B, Ban E, Park J, Song Y and Kim CJ Liq: Chromatogram. Related. Technol 2005; 27: 3089–3102.
6. British Pharmacopoeia (2021). British Pharmacopoeia Commission. London: TSO.
7. Chan V: (2015, December 16). Experiment 1: Uniformity of diameter, thickness and hardness. Saya Sayang UKM Farmasi. https://sayasayangukmfarmasi.wordpress.com/2015/12/17/experiment-1-uniformity-of-diameter- thickness-and hardness/#:~:text=Meanwhile%2C%20the%20diameter%20of%20tablets
8. Chen WL, Guo DW, Shen YY, Guo SR & Ruan KP: Effects ofHighly Hygroscopic Excipients on the Hydrolysis of Simvastatin in Tablet at High Relative Humidity. Indian Journal of Pharmaceutical Sciences, 2012; 74(6): 527–534. https://doi.org/10.4103/0250-474X.110587
9. Cordeiro T, Matos I, Danede F, Sotomayor J, Fonseca I, Corvo MC, Madalena Dionisio, María Teresa Viciosa, Fredeic Affouard & Correia NT: Evidence of Strong Guest–Host Interactions in Simvastatin Loaded in Mesoporous Silica MCM- 41. Pharmaceutics 2023; 15(5): 1320–1320. https://doi.org/10.3390/pharmaceutics15051320
10. Don: (2012, May 9). Pharma Treasures: Tablet weight variation and uniformity of weight of single dose preparations - Pharmacopeal requirements IP/BP/USP. Pharma Treasures. http://pharmatreasures.blogspot.com/2012/05/tablet-weight-variation-and-uniformity.html
11. Elawni and Alaa: (2016). What affect air bubbles upon dissolution testing. https://www.researchgate.net/post/What-affect-air-bubbles-upon-dissolution-testing/576e5af65b495262c8457613/citation/download
12. Elena B, Rosa P & Regina M: Assessment of the quality of simvastatin capsules from compounding pharmacies. LA Referencia 2010; 44(6): 1055–1062.
13. Eyad SM. Abu-Nameh, Reyad Shawabkeh & Ali A: High-performance liquid chromatographic determination of simvastatin in medical drugs. Journal of Analytical Chemistry 2006; 61(1): 63–66. https://doi.org/10.1134/s1061934806010138
14. Fatima S, Usman S & Iyad Naeem Muhammad: Statistical Evaluation of In-Vitro Dissolution Profiles of Different Brands of Simvastatin 20 mg Tablets Available In Local Market of Karachi. International Journal of Pharmacy and Pharmaceutical Sciences 2013; 5(3): 622- 626.
15. Ghimire Prakash, Shrestha Abinash Chandra, Pandey Sandhya, Chapagain Bidur & Dhakal Samir. Pharmacopoeial comparison of in-process and finished product quality control test for pharmaceutical tablets. GSC Biological and Pharmaceutical Sciences 2020; 11(3): 155–165; https://doi.org/10.30574/gscbps.2020.11.3.0174
16. Graeser KA, Strachan CJ, Patterson JE, Gordon KC & Rades T: Physicochemical Properties and Stability of Two Differently Prepared Amorphous Forms of Simvastatin. Crystal Growth & Design 2008; 8(1): 128–135. https://doi.org/10.1021/cg700913m
17. Guzik Ł, Mrozik W & Kamysz W: Determination of Simvastatin in Pharmaceutical Dosage Forms by Optimized and Validated Method Using HPLC/UV. Croatica Chemica Acta 2010; 83(4): 371–377.

18. Haaren C, De Bock M & Kazarian SG: Advances in ATR-FTIR Spectroscopic Imaging for the Analysis of Tablet Dissolution and Drug Release. Molecules 2023; 28(12): 4705.https://doi.org/10.3390/molecules28124705
19. Heidari A: Fourier Transform Infrared (FTIR) Spectroscopy, Global Imaging Insights 2018; 3(2): https://doi.org/10.15761/gii.1000153.
20. Ibide dissolution procedure (2011): development and validation. Rockville: UnitedStates Pharmacopeial Convention.
21. Iyan Sopyan, Muhammad Raihan Riyaldi, Soraya Ratnawulan Mita & Iyan Sopyan: Increasing solution in the drug simvastatin with solid dispersion technique using polymer soluplus. International Journal of Applied Pharmaceutics 2023; 15(4): 160–165. https://doi.org/10.22159/ijap.2023v15i4.48293
22. Juan Manuel Aceves-Hernández, J. Hinojosa-Torres, María Ines Nicolas-Vazquez, Rene Miranda Ruvalcaba, & María R: Solubility of simvastatin: A theoretical and experimental study. Journal of Molecular Structure 2011; 995(1-3): 41–50. https://doi.org/10.1016/j.molstruc.2011.03.048
23. Kesharwani D, Mishra S, Paul SD, Paliwal R & Satapathy T: Solubility augmentation of simvastatin by using the marvelous carrier hydroxy propyl beta- cyclodextrin: compatibility study, statistical and spectral analysis. Indian Journal of Pharmaceutical Education and Research 2019; 53(3): 231–238. https://doi.org/10.5530/ijper.53.3s.92.
24. Kim KH, Park JB, Choi WJ, Lee HS & Kang CY: Preparation and Characterization of Simvastatin Solid Dispersion using Aqueous Solvent. Journal of Pharmaceutical Investigation 2011; 41(4): 239–247. https://doi.org/10.4333/kps.2011.41.4.239
25. Lobmann K, Strachan C, Grohganz H, Rades T, Korhonen O & Laitinen R: Co-amorphous simvastatin and glipizide combinations show improved physical stability without evidence of intermolecular interactions. European Journal of Pharmaceutics and Biopharmaceutics 2012; 81(1): 159–169. https://doi.org/10.1016/j.ejpb.2012.02.004
26. Marques-Marinho FD, Santos AL. dos, Vianna-Soares, C. D, Reis IA, Zanon JC. da C & Lima AA: Simvastatin assay and dissolution studies by feasible RP-HPLC in tablets. Química Nova 2012; 35(6): 1233–1238. https://doi.org/10.1590/s0100-40422012000600031
27. Mary Chok Chiew Fong and Azzy Iyzati Ahmad Shanizza: Malaysian Statistics on Medicines 2015-2016. Pharmaceutical Services Programme Ministry of Health Malaysia 2020; 15-17.
28. Melanovic M. Medenica, D. Ivanovic and B. Jancic: Chromatographia 2006; 63.95–100.
29. Miloud el Karbane, Youssef Ramli, Mohammed Amood Al-Kamarany, Bouchfra H, Mohmmed Jabbar Radi, Khalid Karrouchi, Mohamed Azougagh, Yahia Cherrah and Abdelaziz Bouklouze: Development and validation of HPLC dissolution assay of simvastatin tablets under normal and accelerated conditions. Journal of Chemical and Pharmaceutical Research 2014; 6(6): 886-893.
30. Nandi U, Ajiboye AL, Patel P, Douroumis D and Trivedi V: Preparation of solid dispersions of simvastatin and Soluplus using a single-step organic solvent-free supercritical fluid process for the drug solubility and dissolution rate enhancement. Pharmaceuticals (Basel) 2021; 14(9): 846.
31. Patel D, Patel U, Shukla M, Bhimani B & Patel G: Formulation and Evaluation of Immediate Release Tablet of Simvastatin. Research Journal of Pharmacy and Technology 2020; 13(1): 421. https://doi.org/10.5958/0974-360x.2020.00082.7
32. Rahamathulla M, HV G, Veerapu G, Hani U, Alhamhoom, Y, Alqahtani A & Moin: Characterization, optimization, *in-vitro* and *in-vivo* evaluation of simvastatin proliposomes, as a drug delivery. Pharm Sci Tech 2020; 21(4). https://doi.org/10.1208/s12249- 020-01666-4
33. Sakina Fatima, Shahnaz Usman and Subia Jamil: EFFECT OF Surfactanton Dissolution of Simvastatin Tablets; Comparison with USP. World Journal of Pharmacy and Pharmaceutical Sciences 2014; 3(3): 142–150.
34. Singh H, Philip B & Pathak K: Preparation, Characterization and Pharmacodynamic Evaluation of Fused Dispersions of Simvastatin using PEO-PPOBlock Copolymer. PubMed 2012; 11(2): 433–445.
35. Sopyan I, Pallanisamy T and Wardhana YW: Polymorpism of simvastatin: an effort to repair solubility and dissolution rate. Pharm Lett 2017; 9(6): 18-27.
36. Szilard Zsolt Farkas, Silvia Imre, Daniela-Lucia Muntean and Amelia Tero-Vescan: Analysia of Drug Related Impurities by Infrared Spectrometry in the Class of Statins. Farmacia 2013; 61(6): 1091–1101.
37. Talreja O & Cassagnol M: Simvastatin. Nih.gov; Stat Pearls Publishing 2019. https://www.ncbi.nlm.nih.gov/books/NBK532919/
38. Tamader Y. Elghnimi, Mosbah A. El-Majri, Redab Bennouh, Aya Enkessa and Mohamed M. Siaan: Comparative In-Vitro Evaluation of Commercial Simvastatin Tablets (20 mg). Inter J of Pharmaceutical Sciences and Research 2016; 7(6): 2402–24

How to cite this article:
Yi LZ, Perveen N, Varghese N and Khan NH: Quality assessment and comparative study of different marketed brands of simvastatin in malaysia. Int J Pharm Sci & Res 2025; 16(1): 241-57. doi: 10.13040/IJPSR.0975-8232.16(1).241-57.