

EQUIVALENCE OF VARIOUS BRANDS OF AMLODIPINE BESYLATE (5 MG) TABLETS IN BIOWAIVER CONDITION

Krishna Neupane, Anil Bhusal*, Sandeep Pandit, Santosh Dhungana, Sujan Khadka, Sajan Maharjan

Department of Pharmacy, Central Institute of Science and Technology (CiST College), Affiliated to Pokhara University,
New Baneshwor, Kathmandu, Nepal.

Article Received: 04 August 2026 | Article Revised: 25 August 2026 | Article Accepted: 14 September 2026

***Corresponding Author: Anil Bhusal**

Department of Pharmacy, Central Institute of Science and Technology (CiST College), Affiliated to Pokhara University, New Baneshwor,
Kathmandu, Nepal. DOI: <https://doi.org/10.5281/zenodo.22794637>

How to cite this Article: Krishna Neupane, Anil Bhusal, Sandeep Pandit, Santosh Dhungana, Sujan Khadka, Sajan Maharjan (2026)
EQUIVALENCE OF VARIOUS BRANDS OF AMLODIPINE BESYLATE (5 MG) TABLETS IN BIOWAIVER CONDITION. World Journal
of Pharmaceutical Science and Research, 5(9), 759-771.



Copyright © 2026 Anil Bhusal | World Journal of Pharmaceutical Science and Research.

This work is licensed under creative Commons Attribution-NonCommercial 4.0 International license (CC BY-NC 4.0).

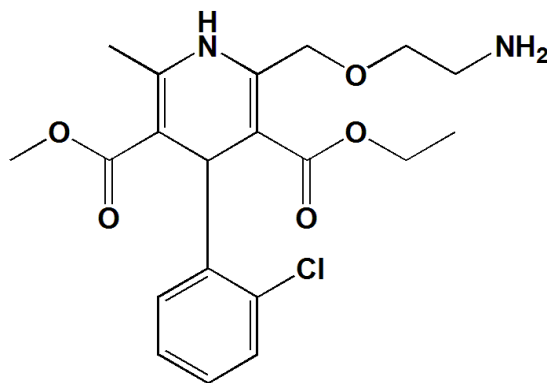
ABSTRACT

Background: A biowaiver based on the Biopharmaceutics Classification System (BCS) allows in vivo bioequivalence testing to be replaced by comparative in vitro dissolution for immediate-release solid oral dosage forms containing highly soluble and highly permeable drugs. Amlodipine besylate is classified as a BCS Class I drug and therefore qualifies for this approach. More than 40 Nepali manufacturers market amlodipine, but the quality and interchangeability of these products had not previously been assessed. **Objective:** To evaluate the pharmaceutical quality of amlodipine besylate (5 mg) tablets available in the Nepali market and to assess their equivalence with the innovator product under biowaiver conditions. **Materials and Methods:** Eight generic amlodipine besylate 5 mg tablet brands were randomly collected from hospital, retail and community pharmacies in Nepal and coded A to H. The innovator product (Pfizer), coded I, was obtained from India and used as the reference. Weight variation, hardness and drug content were determined, the last by a UV spectrophotometric method at 240 nm against a calibration curve prepared from standard amlodipine. In vitro dissolution was carried out on 12 tablets per brand using USP apparatus 2 at 75 rpm in 900 mL of three media (0.1 N HCl pH 1.2, acetate buffer pH 4.5 and phosphate buffer pH 6.8) at 37 ± 2 °C, with sampling at 10, 15, 20, 30 and 45 minutes. Dissolution profiles of each generic were compared with the innovator using the difference factor (f_1) and similarity factor (f_2), with similarity accepted at $f_1 \leq 15$ and $f_2 \geq 50$. **Results:** Average tablet weights ranged from 0.11 to 0.19 g and hardness from 1.5 to 5 kg/cm², with no marked differences between brands. Drug content ranged from 86.87 % to 124.13 %. Two of the eight generics fell outside the USP acceptance range of 90–110 %: brand G at 86.87 % and brand D at 124.13 %. At 45 minutes, all products released more than 88 % of the labelled amount in every medium, and several values exceeded 100 %. Profile comparison gave a different picture from the endpoint data. Brand B showed the closest agreement with the innovator (f_2 of 72, 79 and 77 at pH 1.2, 4.5 and 6.8), followed by brand H (59, 66 and 85). Brand C failed the similarity criterion in all three media (f_2 of 43, 34 and 46), and brands A and F each failed in one medium. Products that met the criteria in all three media were therefore a minority, even though nearly all products had released most of the drug by 45 minutes. **Conclusion:** Within the conditions of this study, all brands met the physical quality tests, but two failed the content uniformity requirement and only a small number matched the innovator dissolution profile across all three media. The findings indicate that not all amlodipine generics on the Nepali market can be assumed to be interchangeable with the innovator, and support the need for routine post-marketing quality assessment.

KEYWORDS: Biowaiver, Amlodipine besylate, Dissolution, Similarity factor, Generic substitution.

INTRODUCTION

Amlodipine is a dihydropyridine calcium channel blocker used alone or with other medicines to treat hypertension and angina.^[1] It lowers blood pressure by relaxing the blood vessels so that the heart does not have to pump as hard, and it relieves chest pain by increasing blood supply to the heart. Taken regularly it controls angina, although it does not relieve an attack once it has started. Its chemical name is 3-O-ethyl 5-O-methyl 2-(2-aminoethyl methyl)-4-(2-chlorophenyl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate,^[2] and its structure is shown in Figure 1. Because hypertension requires lifelong treatment, amlodipine is listed in the WHO Model List of Essential Medicines as a 5 mg tablet,^[3] and in Nepal it holds marketing authorisation as an immediate-release tablet in 2.5, 5 and 10 mg strengths.^[4]



Amlodipine

Figure 1: Structure of amlodipine.

Long-term therapy of this kind is usually supplied by generic products, and their quality determines whether treatment succeeds. WHO has estimated that about 10 % of medical products in low- and middle-income countries are substandard or falsified, and that these products reach patients most often where access to quality medicines is limited, technical capacity is weak and governance is poor.^[5] A substandard product is an authorised product that fails to meet its specifications, while a falsified product misrepresents its source, composition or identity. Either may fail to treat the condition for which it was given, and may harm the patient. Generic substitution rests on the assumption that a pharmaceutically equivalent product will show the same clinical safety and efficacy as the brand it replaces.^[6] That assumption has to be tested rather than taken for granted, particularly where price is the main basis for product selection.

Comparative dissolution testing is the usual way of testing it without recourse to human studies. A biowaiver is the regulatory acceptance of in vitro dissolution data in place of an in vivo bioequivalence study, on the condition that dissolution reliably predicts in vivo behaviour.^[7] The BCS provides the framework for deciding when this condition holds up.^[7] A drug substance is considered highly soluble when its highest dose strength dissolves in less than 250 mL of water over pH 1 to 7.5, and highly permeable when more than 90 % of an administered dose is absorbed. An immediate-release product is considered rapidly dissolving when not less than 85 % of the labelled amount dissolves within 30 minutes in each of the three physiologically relevant media.^[8] Amlodipine satisfies the substance-level criteria: it is slightly soluble in water but freely soluble in methanol,^[9] with a reported aqueous solubility of 2.6 mg/mL in distilled water,^[10] and as a weak base it remains ionised and highly soluble across the pH 1 to 6.8 range of the gastrointestinal tract.^[11] It is accordingly assigned to BCS Class I.^[12] What the BCS classification cannot establish is

whether a particular manufactured product releases the drug in the same way as the reference, and that is what dissolution testing has to determine for each brand.

Amlodipine has been examined under biowaiver conditions in several countries, with results that differ enough to make local testing necessary.^[13] Studied tablets marketed in Russia according to WHO guidance, and carried out a comparable assessment. Reported that six brands available in Pakistan all released more than 85 % of the drug within 15 minutes, so that profile comparison was not required and all the generics tested were judged interchangeable with the innovator. Reached a different conclusion for two brands in Nigeria: none met the criteria for very rapidly dissolving tablets, and only one of the two generics was comparable with the innovator in all media.^[11,14] Since products, excipients and manufacturing practices differ from one market to another, findings from one country cannot be transferred to another.

More than 40 Nepali companies market an amlodipine product, and no such study had been carried out on amlodipine tablets in Nepal.^[15] The present study was therefore undertaken to evaluate the pharmaceutical quality of generic amlodipine besylate (5 mg) tablets available in the Nepali market through weight variation, hardness and assay testing, and to compare their in vitro dissolution profiles with the innovator product from Pfizer in three dissolution media using the difference and similarity factors, in order to assess whether these products can reasonably be substituted for the innovator under biowaiver conditions.^[16]

MATERIALS AND METHODS

Study Design, Site and Duration

An experimental laboratory study was carried out in the laboratory of the Central Institute of Science and Technology (CiST) College, Kathmandu, from May to June 2022.

Product Selection and Sampling

Information on the amlodipine products registered in the country was obtained from the Department of Drug Administration. More than 60 amlodipine products are available in Nepal, of which 40 are manufactured by Nepali pharmaceutical companies.^[15] Eight products of Nepali manufacture were selected at random from hospital, retail and community pharmacies and coded A to H, the brand names being withheld throughout. Only Amlodipine 5 mg single-ingredient tablets were included; fixed-dose combinations were excluded. The innovator product from Pfizer was purchased from India and coded I, and served as the reference against which all generics were compared. All products were within their labelled shelf life at the time of testing.

Materials and Equipment

Standard amlodipine was obtained from SR Pharmaceuticals and used to prepare the standard solutions for assay and dissolution. Methanol was used for sample preparation. Concentrated HCl (pH 1.2), acetate buffer (pH 4.5) and phosphate buffer (pH 6.8) were used as dissolution media, and sodium hydroxide for buffer preparation.^[17] The instruments used are listed in Table 1.

Table 1: Instruments and equipment used.

Instrument	Specification
UV-visible spectrophotometer	SHIMADZU CORP, UV-1800, Serial A114548
Dissolution apparatus	Optics Technology (ISO 9001:2008 certified), Model DA-6S
Sonicator	Ultrasonic cleaner, DAIHAN Scientific
Weighing balance	PHOENIX Instrument, Model PH3203CHE, precision 1 mg, capacity 320 g
Centrifuge	4000 rpm
pH meter	Digital portable pH meter, Model CPH102
Glassware	Borosilicate grade

Calibration verification was performed as per USP for both the dissolution apparatus and the UV spectrophotometer before use.

Physical Testing

All nine products, generic and innovator, were subjected to weight variation and hardness testing according to established protocols. Tablets were weighed individually on the validated analytical balance and the mean and standard deviation calculated for each brand.

Analytical Method and Assay

A stock standard solution was prepared by dissolving an appropriate quantity of amlodipine besylate in a small volume of methanol with the aid of sonication, and making up to volume with 0.01 N HCl to give a concentration of 100 µg/L. Calibration standards of 2, 5, 10 and 20 µg/mL were prepared in 0.01 N HCl in triplicate. Absorbance was measured at 240 nm and the calibration curve constructed by plotting absorbance against concentration, followed by regression analysis and determination of the correlation coefficient.^[18] Intra-day and inter-day precision and accuracy were established using quality control samples at low (2 µg/mL), mid (10 µg/mL) and high (20 µg/mL) concentrations, prepared in triplicate from amlodipine besylate tablet powder. Solution stability was assessed by re-analysing the 10 µg/mL working solution after standing at laboratory temperature ($25 \pm 2^\circ\text{C}$) for at least 12 hours.

For the assay, tablets were crushed to a fine powder and a quantity equivalent to 5 mg of amlodipine was taken. The powder was sonicated in 5 mL of methanol for 10 minutes at room temperature, made up to 50 mL with 0.01 N HCl and sonicated for a further 5 minutes. The mixture was filtered through a 0.45 µm nylon filter and diluted with 0.01 N HCl to 10 µg/mL.^[19] Absorbance was recorded at 240 nm in triplicate and the content calculated from the calibration curve. Products were considered to comply if the assay result fell within 90–110 % of the labelled amount.^[20]

In Vitro Dissolution Testing

Dissolution was performed using USP apparatus 2 (paddle) on 12 tablets per product in 900 mL of medium at 75 rpm and $37 \pm 2^\circ\text{C}$, following the procedure of the USP-NF monograph for amlodipine immediate-release tablets and the WHO and US FDA biowaiver guidelines (21) (22). Three media were used: 0.1 N HCl (pH 1.2, simulated gastric fluid without enzyme), acetate buffer (pH 4.5), and phosphate buffer (pH 6.8, simulated intestinal fluid without enzyme).^[17] Because amlodipine is light sensitive, the dissolution vessels were wrapped in aluminium foil throughout the test.^[23]

Aliquots of 5 mL were withdrawn at 10, 15, 20, 30 and 45 minutes and immediately replaced with an equal volume of fresh medium pre-equilibrated to 37°C to maintain sink conditions. Samples were filtered through a 0.45 µm nylon filter and the absorbance read at 240 nm against the corresponding dissolution medium as blank.^[18] The percentage of drug released at each time point was calculated from the standard calibration curve.

RESULTS AND DISCUSSION

Amlodipine besylate is classified as a BCS Class I drug and so qualifies in principle for a biowaiver, which is why this study assessed equivalence through comparative dissolution rather than through in vivo testing. The results show that qualifying in principle is not the same as qualifying in practice, and that the outcome depends heavily on which criterion is applied.

General Characteristics of the Tested Brands

The label information of the eight generic brands is given in Table 2. Prices were uniform at NPR 50 per 10 tablets for seven of the eight products, with brand B slightly cheaper at NPR 40.

Table 2: Label information of the tested amlodipine products.

S.N	Brand code	Manufacturing date	Expiry date
1	A	Feb. 2022	Jan-24
2	B	Feb-21	Jan-23
3	C	Nov-20	Oct-22
4	D	Dec-21	Nov-23
5	E	Jan-21	Dec-22
6	F	Apr-21	Mar-23
7	G	21-Apr	Mar-23
8	H	May-21	Apr-23

The physical and chemical characteristics of all nine products are summarised in Table 3.

Table 3: Physicochemical properties of the tested amlodipine products.

Brand	Average weight (g)	Average weight $\pm$ SD (g)	Hardness (kg/cm ²)	Drug content (%)
A	0.19	0.1924 $\pm$ 0.00196	3	108.24
B	0.16	0.1642 $\pm$ 0.0016	3.2	97.33
C	0.11	0.111 $\pm$ 0.001095	2.5	97.87
D	0.11	0.1118 $\pm$ 0.002786	3.7	124.13
E	0.13	0.1328 $\pm$ 0.001939	2.5	100.12
F	0.17	0.171 $\pm$ 0.001414	3.8	97.85
G	0.16	0.1606 $\pm$ 0.001744	5	86.87
H	0.11	0.1178 $\pm$ 0.0098	4	97.85
I (innovator)	0.19	0.1976 $\pm$ 0.0016	1.5	100.69

Tablet weights varied nearly twofold between products, from 0.11 g to about 0.19 g, which reflects differences in the amount and type of excipient used rather than any difference in drug loading, since all products contain the same 5 mg strength. Within each brand the weights were consistent, with small standard deviations; brand H was the exception, showing a standard deviation several times larger than that of the other products relative to its mean. Hardness ranged from 1.5 to 5 kg/cm², the innovator being the softest tablet tested and brand G the hardest. No brand was outside the range that would be expected for an immediate-release tablet.

The physical tests raised no concerns. Weight and hardness were consistent within each brand and none of the values fell outside what would be expected for an immediate-release tablet. The nearly twofold spread in tablet weight between brands reflects differences in formulation rather than in drug content, since all products carry the same 5 mg of amlodipine, and such differences are normal among multisource products. It is worth noting that the innovator was the softest tablet at 1.5 kg/cm² yet gave one of the more consistent dissolution results, while brand G was the hardest at 5

kg/cm² and still released more than 89 % in every medium. Hardness within this range therefore did not predict dissolution behaviour, and physical testing alone would not have identified any of the problems found later.

Drug Content

Drug content ranged from 86.87 % to 124.13 % of the labelled amount (Figure 2). Seven of the nine products, including the innovator at 100.69 %, fell within the USP acceptance range of 90–110 %. Two generics did not: brand G contained 86.87 %, below the lower limit, and brand D contained 124.13 %, well above the upper limit. Brand A at 108.24 % was within the range but towards its upper end.

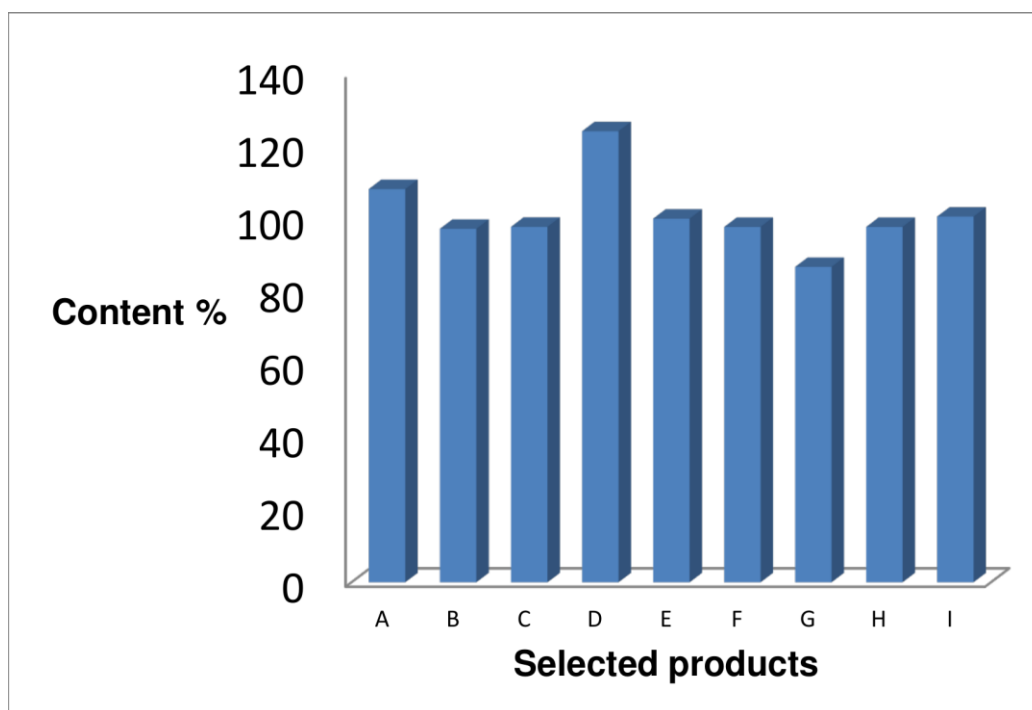


Figure 2: Drug content of each amlodipine product.

The deviation seen in brand D is the larger of the two and is the more difficult to account for by ordinary manufacturing variation. A content of 124 % of label represents roughly a quarter more drug than declared, which points to a problem in blending or in the assay itself rather than to routine batch variability.

The assay results were a different matter. Brand G at 86.87 % and brand D at 124.13 % both fell outside the USP range of 90–110 %, meaning that two of eight generics did not deliver the labelled dose. The clinical significance differs between the two. A product containing 86.87 % of label delivers less drug than intended, and for an antihypertensive taken daily over years this could contribute to inadequate blood pressure control that would be difficult to distinguish from poor adherence or inadequate dosing. A product containing 124.13 % delivers about a quarter more drug than intended, which carries the opposite risk. Amlodipine has a wide therapeutic index, so neither deviation is likely to be dangerous in a single dose, but both undermine the assumption on which substitution rests, that the patient receives the same amount of drug regardless of which brand is dispensed. The magnitude of the deviation in brand D is also difficult to attribute to normal manufacturing variability, and points either to a blending or content uniformity problem at manufacture or to interference in the assay.

That second possibility deserves attention because the dissolution data show a similar pattern. Six of the nine products gave release values above 100 % in at least one medium, reaching 115.71 % for brand E at pH 6.8. Release cannot exceed the amount of drug actually present, so these values indicate either that the products contain more drug than labelled or that the analytical method overestimates the amount released. Since the assay for most of these products was close to 100 %, method-related overestimation is the more likely explanation for the majority of them. UV detection at a single wavelength cannot distinguish the drug from excipients or degradation products that absorb at the same wavelength, and the sequential replacement of withdrawn medium introduces further error into the cumulative calculation.

The research attributes the discrepancies between products to variability or instrumental error, and the pattern of above-100 % values supports that interpretation, particularly for brand D where an assay of 124.13 % and dissolution values of about 110 % point in the same direction.

Dissolution Behaviour

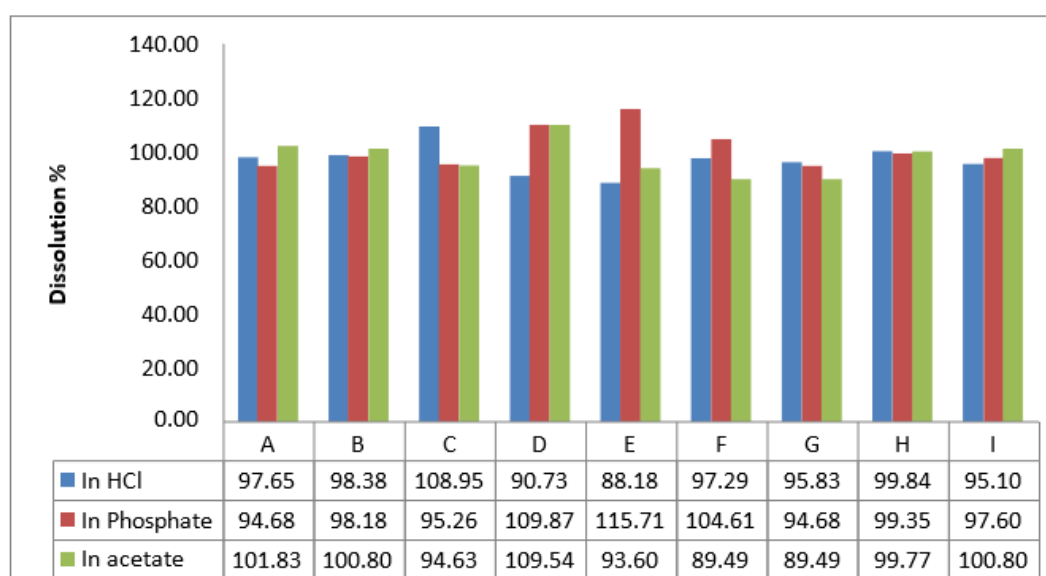


Figure 3: Dissolution % of amlodipine products after 45 minutes.

Figure 4 represents the dissolution profiles comparison and corresponding data of the three formulations in dissolution medium pH 1.2, 4.5 and 6.8. The dissolution profile of Amlodipine tablets was evaluated in 900mL of 0.1NHCl and buffer pH 4.5 acetate buffer and 6.8 phosphate buffer using US Pharmacopoeia dissolution apparatus II. In order to avoid degradation of amlodipine and to maintain optimum dissolution values, the experiments were carried out by wrapping the dissolution vessels in aluminum foil to exclude effect of light. The temperature and degree of agitation were set at $37\text{C}\pm 0.5$ and 75 revolutions per minute respectively. Sample (5.0ml) was collected at predetermined time intervals 5, 10, 15, 20,30 and 45 minutes. 5ml of fresh medium already equilibrated to 37°C was replaced into dissolution medium after each sampling in order to maintain sink condition. Twelve tablets per brand were used for the study. The collected samples were filtered with syringe filter $0.45\mu\text{m}$ (Millipore) to remove any insoluble excipients. The filtered samples were analyzed by the validated Ultra-violet spectrophotometric method (UV) at 240nm wavelength.

The percentage of drug released at 45 minutes in each medium is presented in Table 4.

Table 4: Drug released at 45 minutes (%) in the three dissolution media.

Brand	pH 1.2 (0.1 N HCl)	pH 4.5 (acetate)	pH 6.8 (phosphate)
A	97.65	101.83	94.68
B	98.38	100.80	98.18
C	108.95	94.63	95.26
D	90.73	109.54	109.87
E	88.18	93.60	115.71
F	97.29	89.49	104.61
G	95.83	89.49	94.68
H	99.84	99.77	99.35
I (innovator)	95.10	100.80	97.60

By 45 minutes every product had released more than 88 % of the labelled amount in every medium, so on the extent of release alone no product would be excluded. Several values exceeded 100 %, the highest being 115.71 % for brand E at pH 6.8, and values above 100 % were recorded for six of the nine products in at least one medium. Brand H gave the most consistent result across media, releasing between 99.35 % and 99.84 % in all three, while brands D, E and F varied by 15 percentage points or more depending on the medium.

The dissolution profiles in the three media are shown in Figures 3 to 5. In 0.1 N HCl at pH 1.2 most products met the criterion of 85 % or more released within 20 minutes. In acetate buffer at pH 4.5 most products met the criterion but two did not, and in phosphate buffer at pH 6.8 brand A did not. Because not all products qualified as very rapidly dissolving in all media, the exemption from profile comparison could not be applied and the similarity factors were calculated.

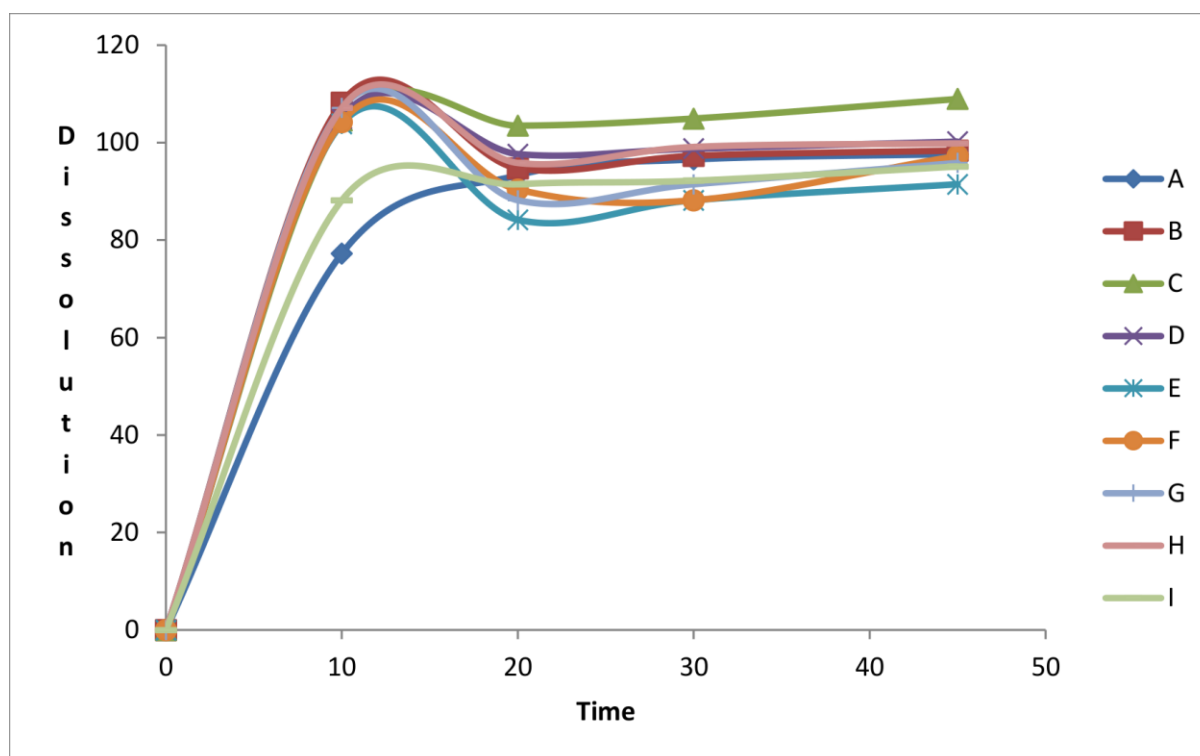


Figure 4: Dissolution profiles of the tested brands at pH 1.2.

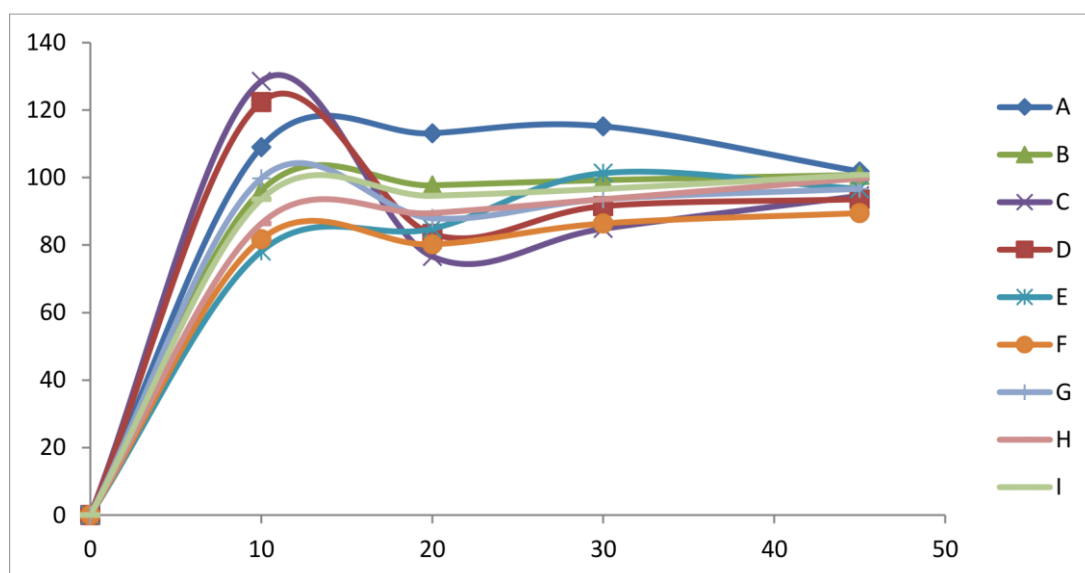


Figure 5: Dissolution profiles of the tested brands at pH 4.5.

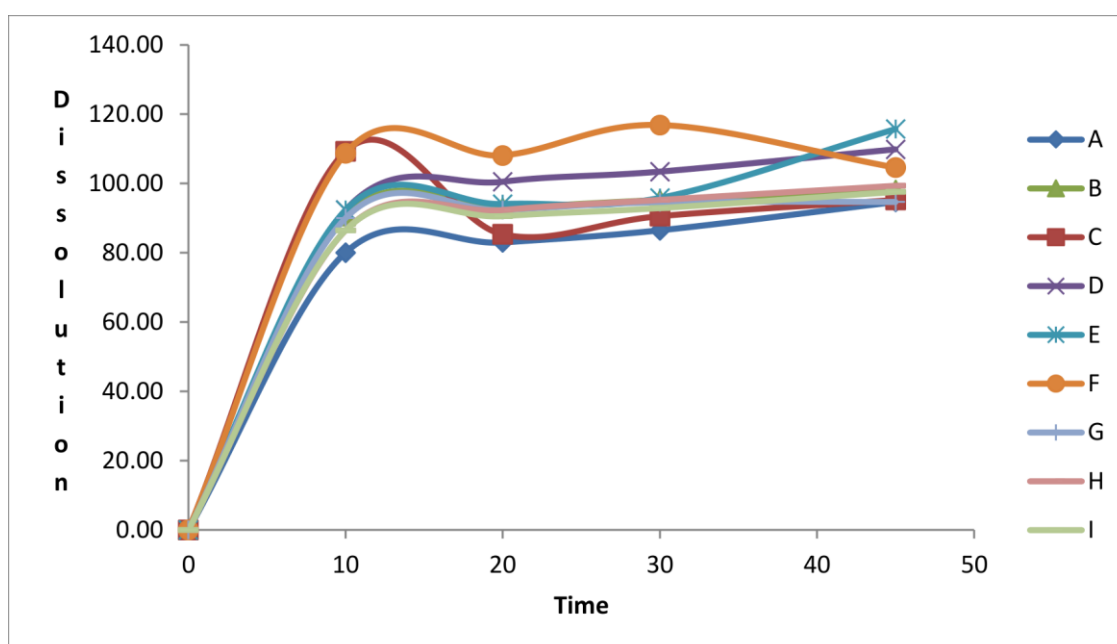


Figure 6: Dissolution profiles of the tested brands at pH 6.8.

Similarity Assessment

The difference and similarity factors for each generic against the innovator are given in Table 5.

Table 5: Difference (f1) and similarity (f2) factors of the tested brands relative to the innovator.

Brand	pH 1.2 f1	pH 1.2 f2	pH 4.5 f1	pH 4.5 f2	pH 6.8 f1	pH 6.8 f2
A	5	60	14	41	6	60
B	3	72	2	79	3	77
C	15	43	18	34	9	46
D	9	50	14	40	10	50
E	8	52	9	51	8	50
F	6	54	12	46	13	39
G	6	49	12	64	3	78
H	10	59	4	66	2	85

Brand B gave the highest similarity factors of any product, between 72 and 79 across the three media, and the lowest difference factors, between 2 and 3. Brand H was next, with f_2 rising from 59 at pH 1.2 to 85 at pH 6.8. At the other extreme, brand C failed the f_2 criterion in all three media and also breached the f_1 limit of 15 at pH 1.2 and pH 4.5, making it the least similar product tested. Brands A and F each fell below f_2 of 50 in a single medium — brand A at pH 4.5 and brand F at pH 6.8 — while meeting the criterion in the other two. Brand D was borderline, exactly at f_2 of 50 in two media and below it in the third, and brand G fell just short at pH 1.2 with an f_2 of 49 while performing well in the other two media.

The most useful finding concerns the gap between the two ways of judging equivalence. By 45 minutes every product had released more than 88 % of label in every medium, which by itself would suggest that all the products behave alike. The similarity factors show that they do not. Brand C illustrates the point: it released 108.95 %, 94.63 % and 95.26 % at 45 minutes, comparable to any other product, yet failed the f_2 criterion in all three media and also exceeded the f_1 limit at two of them. The difference between brand C and the innovator therefore lies not in how much drug is eventually released but in how quickly it is released during the early part of the test, which is exactly what f_2 is designed to detect and what an endpoint measurement cannot. The same applies to brand A, which recorded the highest 45-minute value of all products at pH 4.5 but had an f_2 of only 41 in that medium. This is the practical reason why regulatory guidance requires profile comparison rather than a single-point specification for products that are not very rapidly dissolving.

Applying the criteria stated in the methods, brand B matched the innovator most closely, with f_2 values between 72 and 79 and f_1 values of 2 to 3 in all three media, a degree of agreement that leaves little doubt about its dissolution behaviour. Brand H also met the criterion in all three media, with the agreement improving as pH rose to reach an f_2 of 85 at pH 6.8. Brand E met the criterion in all three media but only just, with f_2 values of 52, 51 and 50, which sit close enough to the boundary that a repeat experiment could plausibly place them on either side of it. Brands A, D, F and G each failed in at least one medium, and brand C in all three. Within the conditions of this study, the findings therefore support the interchangeability of brand B with the innovator, and support that of brand H, while indicating that the remaining products cannot be assumed interchangeable on the evidence available. It should be said plainly that failing an f_2 comparison is not the same as being therapeutically inequivalent; it means that in vitro data alone do not establish equivalence, and that the biowaiver route is not available for that product.

These results sit between the two published studies most directly comparable. Feroz et al.^[13] found that all six brands they tested in Pakistan released more than 85 % within 15 minutes in every medium, so that they qualified as very rapidly dissolving and profile comparison was not required at all, and they concluded that all the generics were interchangeable with the innovator. No such conclusion is possible for the Nepali products tested here: not all of them met the 85 % in 20 minutes criterion in every medium, which is precisely why the similarity factors had to be calculated. Akinleye et al.^[14] reported for two Nigerian brands that neither met the criteria for very rapidly dissolving tablets and that one of the two had an f_2 below 50 in one medium while the other was comparable in all media. The present findings resemble the Nigerian study far more closely than the Pakistani one, both in the failure of products to qualify as very rapidly dissolving and in the pattern of some products passing in most media but failing in one. Whether this reflects genuine differences in product quality between these markets or differences in analytical conditions cannot be determined from the available data, since the three studies used different equipment and, in the case of Feroz et al., a fourth medium of distilled water and a wider set of sampling times.

Some caution is needed in interpreting the similarity factors themselves. The f_2 statistic loses discriminating power when several sampling points lie above 85 % dissolution, because differences between two curves that have both plateaued are small and the calculation returns a high value regardless. Given how rapidly these products released the drug, several of the comparisons will have included multiple points above 85 %, which means the reported f_2 values may if anything be generous to the test products. This makes the failure of brand C in all three media more rather than less notable.

Two of the products with content outside specification, brands D and G, were retained in the dissolution comparison. This is defensible as a description of what is actually on the market, but it complicates interpretation, because a dissolution profile expressed as a percentage of the labelled amount will be shifted for a product whose true content differs from the label. For brand D in particular, the elevated dissolution values at pH 4.5 and 6.8 are consistent with its elevated content, and its f_2 results cannot be separated cleanly from its content problem.

Overall Equivalence Assessment

Taken together, the two sets of results point in different directions. Judged only by the extent of release at 45 minutes, every product performed acceptably. Judged by profile comparison against the innovator, the products separate clearly: brand B matched the innovator closely in all three media, brand H matched it well and improved as pH rose, brand E met the criterion but only marginally, and the remaining products failed in at least one medium. Of the two products that failed the content uniformity test, neither met the similarity criteria in all three media.

Beyond the individual products, the wider finding is that quality among amlodipine generics in Nepal is not uniform. Two of eight failed a compendial content requirement and only a minority matched the innovator profile across all three media. Since more than 40 Nepali manufacturers market this drug and no previous assessment of these products existed, the results indicate a need for routine post-marketing surveillance rather than reliance on registration data alone. They also have a practical bearing on substitution at the pharmacy counter. Prices in this sample were almost uniform, so cost gave no useful signal about quality, and the products that performed best were not distinguishable from the others by price, packaging or physical appearance. Prescribers and pharmacists cannot identify a well-performing generic without the kind of data generated here, which is an argument for regulatory bodies to generate and publish it.

CONCLUSION

All eight generic amlodipine besylate (5 mg) brands tested met the physical quality requirements, but two of them, brands D and G, fell outside the USP content limits of 90–110 %. Although every product released more than 88 % of the labelled amount by 45 minutes in all three media, comparison of the full dissolution profiles against the innovator gave a more discriminating result: brand B matched the innovator closely in all three media, brand H also met the similarity criteria, brand E met them marginally, and the remaining brands failed in at least one medium, with brand C failing in all three. Within the conditions of this study, the findings support the substitution of brand B, and of brand H, for the innovator, but do not support the assumption that amlodipine generics on the Nepali market are interchangeable as a class. Regular post-marketing quality assessment, and the publication of such data by the regulatory authority, would give prescribers and pharmacists a sounder basis for generic selection than price or availability.

Ethical Consideration

Ethical approval for the study was obtained from the Institutional Review Committee of CiST College, Pokhara University.

REFERENCES

1. Eisenberg MJ, Brox A, Bestawros AN. Calcium channel blockers: an update. *Am J Med*, 2004; 116(1): 35–43.
2. Kaynak MS, Bogacz A, Stelmasinski M, Sahin S. Bioavailability File: Amlodipine/Biyoyararlanım Dosyası: Amlodipin. *FABAD J Pharm Sci*, 2011; 36(4): 207.
3. Preparations WEC on S for P. WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-third report. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: Thirty-third report [Internet], 1993; [cited 2026 Aug 31]; p. 30–30. Available from: <https://pesquisa.bvsalud.org/portal/resource/pt/pah-14712>
4. Pant T, Mishra K, Subedi RK. In vitro studies of amlodipine besylate tablet and comparison with foreign brand leader in Nepal. *Int J Pharm Sci Res*, 2013; 4(10): 3958.
5. Popoola OO, Madhur G, Mehri MM, Omondi MO, Owusu-Mensah P, Mamtani SA, et al. A Literature Review on the Global Burden and Impact of Substandard and Falsified Medicine. *Ann Public Health Issues*, 2022 Jan 1; 2(1): 16–31. doi:10.2478/aphi-2022-0003
6. Dandam P, Audu-Peter JD. Assessment of the pharmaceutical equivalence and in vitro dissolution studies of amlodipine tablets marketed in Northern Nigeria. *J Pharm Bioresour*, 2020; 17(2): 200–7.
7. Arrunátegui LB, Silva-Barcellos NM, Bellavinha KR, Ev L da S, Souza J de. Biopharmaceutics classification system: importance and inclusion in biowaiver guidance. *Braz J Pharm Sci*, 2015; 51(1): 143–54.
8. Jain S, Patel N, Lin S. Solubility and dissolution enhancement strategies: current understanding and recent trends. *Drug Dev Ind Pharm*, 2015 Jun 3; 41(6): 875–87. doi:10.3109/03639045.2014.971027
9. Anderson S. Pharmacy and empire: The "British Pharmacopoeia" as an instrument of imperialism 1864 to 1932. *Pharm Hist*, 2010; 52(3/4): 112–21.
10. Dahima R, Pachori A, Netam S. Formulation and evaluation of mouth dissolving tablet containing amlodipine besylate solid dispersion. *Int J ChemTech Res*, 2010; 2(1): 706–15.
11. Shohin IE, Ramenskaya GV, Vasilenko GF, Malashenko EA. In Vitro Dissolution Kinetics of Amlodipine Tablets Marketed in Russia Under Biowaiver Conditions. *Dissolution Technol*, 2010; 17(3): 20–2. doi:10.14227/DT170310P20
12. Jung-Cook H, Mayet-Cruz L, Girard-Cuesy ME. Comparative in vitro dissolution and in vivo bioavailability of commercial amlodipine tablets. *Trop J Pharm Res*, 2018; 17(9): 1685–91.
13. Shohin IE, Ramenskaya GV, Vasilenko GF, Malashenko EA. In vitro dissolution kinetics of amlodipine tablets marketed in Russia under biowaiver conditions. *Dissolut Technol*, 2010; 17(3): 20–3.
14. Feroz M, Razvi N, Ghayas S, Anjum F, Ghazal L, Siddiqui SA. Assessment of pharmaceutical quality control and equivalence of various brands of amlodipine besylate (5 mg) tablets available in the Pakistani market under biowaiver conditions. *Int J Pharm Pharm Sci*, 2014; 6(2): 909–13.
15. Gyanwali P, Humagain BR, Aryal KK, Pandit A, Acharya T, Bista B, et al. Surveillance of Quality of Medicines Available in the Nepalese Market: A Study from Kathmandu Valley [Internet]. 2015 [cited 2026 Aug 31]. Available from: <http://103.69.126.140:8080/handle/20.500.14356/1724>

16. Das AK, Chatterjee S, Pal J. Clinical effectiveness and safety of low cost versus innovator brand amlodipine in hypertension: A single-blinded, randomized, crossover, noninferiority trial. *Indian J Pharmacol*, 2016; 48(6): 706.
17. Najmi A, Al Bratty M, Al-Bassam BA, Aseri RA, Wadani TS, Al-Muntashiri AI, et al. Evaluation of in vitro equivalence of commonly available generic brands of amlodipine tablets in Saudi Arabia under biowaiver conditions. *Dissolut Technol* [Internet], 2021 [cited 2026 Aug 31]; 28(2). Available from: <https://www.academia.edu/download/103852228/Amlodipine.pdf>
18. Igboasoyi AC, Egeolu AP, Edet EM. Quality evaluation and UV spectrophotometric assay of ten brands of amlodipine tablets marketed in Uyo, Nigeria. *J Pharm Bioresour*, 2020; 17(1): 60–5.
19. Malesuik MD, Cardoso SG, Bajerski L, Lanzanova FA. Determination of amlodipine in pharmaceutical dosage forms by liquid chromatography and ultraviolet spectrophotometry. *J AOAC Int.*, 2006; 89(2): 359–64.
20. Abdel-Wadood HM, Mohamed NA, Mahmoud AM. Validated spectrofluorometric methods for determination of amlodipine besylate in tablets. *Spectrochim Acta A Mol Biomol Spectrosc*, 2008; 70(3): 564–70.
21. Jaya S, Amala V. Formulation and in vitro evaluation of oral disintegrating tablets of amlodipine besylate. *Int J Appl Pharm*, 2019; 11: 49–54.
22. Davit BM, Kanfer I, Tsang YC, Cardot JM. BCS Biowaivers: Similarities and Differences Among EMA, FDA, and WHO Requirements. *AAPS J.*, 2016 May; 18(3): 612–8. doi:10.1208/s12248-016-9877-2
23. Olayemi SO, Akinleye MO, Awodele EO, Idris O, Oladimeji-Salami J. The physicochemical equivalence of eight brands of amlodipine tablets in Lagos, Nigeria [Internet]. 2012 [cited 2026 Aug 31].