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Original Research Article

Lumefantrine-neusilin® based amorphous multi-component solid dispersion: *In vivo* and *in vitro* characterization

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Abstract

Purpose: *To develop Neusilin-based amorphous multi-component solid dispersions (NAM-SDs) to improve poor aqueous solubility, low bioavailability and absorption of lumefantrine and enhance the antiplasmodial activity.*
Methods: *Solvent evaporation technique was adopted to produce second-generation SDs (N1 - N3); third-generation SDs (N4 - N6 and N10 - N12); and multi-component SDs, NAM-SDs, (N7 - N9 and N13 - N18). In vitro drug release, in vivo anti-plasmodial activity, differential scanning calorimetry (DSC), and wide-angle x-ray diffraction (WAXD) were carried out on the SDs.*
Results: *The highest drug release (80 %) was observed in multi-component SDs (NAM-SDs, formulation N17 containing Kollidon® VA 64). A significant antiplasmodial activity ($p < 0.05$) was observed in mice that received NAM-SDs. The DSC and WAXD studies showed that the formulations solubilized and exhibited an amorphous state.*
Conclusion: *Multi-component amorphous-based lumefantrine SDs (NAM-SDs) may serve as a potential alternative carrier system for oral lumefantrine delivery.*

Keywords: *Multi-component solid dispersion, Lumefantrine, Neusilin®, Kollidon® VA 64, Antiplasmodial*

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INTRODUCTION

Approximately 40 % or more of newly discovered drugs have poor aqueous solubility which poses a serious challenge to the successful development and commercialization of new chemical entities. Class IV of the biopharmaceutical classification system (BCs) is faced with poor solubility and permeability among which is lumefantrine [1]. They display dissolution rate-limited absorption. Thus, researchers are keen to build reliable, scalable, and effective techniques to improve their aqueous solubility. To improve these parameters, different techniques employed by researchers include micronization, solubilization, complexation with polymers, changing physical forms (amorphous), use of prodrugs and drug

derivatization, addition of surfactant, solid dispersion, and so on [2]. Selection of a particular technique depends on the physical and chemical nature of the medicinal agents, polymers, and applications [3]. Among the different techniques, solid dispersions (SDs) have been demonstrated to be the most productive in enhancing dissolution and bioavailability of poorly water-soluble drugs (PWSDs) [4].

The SDs comprise a class of solid formulations of not less than two dissimilar elements, mainly a lipophilic matrix and a lipophobic drug. The matrix may either be crystalline or amorphous. Solid dispersion may enhance the solubility and dissolution of drugs in an aqueous medium. In solid dispersion technology, there is a partial or complete removal of drug crystallinity and molecular dispersion of PWSDs in a hydrophilic polymeric carrier [5,6]. Two basic classifications of solid dispersions (SDs) are based on the molecular arrangement (eutectics, solid solution, microfine crystalline matrix) [3,7] and the carrier matrix used such as first, second, and third generations [8]. The first generation contains crystalline carriers such as urea and sugar [5,9]. The second generation comprises carriers with amorphous nature such as hydroxypropyl methylcellulose [10], while the third generation includes carriers that enhance aqueous solubility such as surfactants, among others [11].

In this study, multi-component SDs were formulated by the inclusion of a carrier, which has additional properties such as crystallization inhibition and hydrophilic solubilizing character. The carrier is kollidon® VA 64. Kollidon® VA 64 is a vinyl pyrrolidone-vinyl acetate copolymer. It is conventionally applied in drug production companies as a binder and a crystallization prohibitor. It is employed in powder granulation and film-forming formulations with adequate plasticity. Lumefantrine is a lipophilic and hydrophobic drug agent used in the management of malaria (plasmodial infections). Malaria has been a public health challenge in tropical and subtropical countries. Lumefantrine belongs to a class IV agent in the BCs and it faces the challenge of poor solubility and permeability. Its bioavailability and absorption are dose-limited.

It has been established that increasing the dose, does not improve bioavailability and absorption [12]. These challenges prompted this study. Multi-component solid dispersion is a solid dispersion consisting of additional excipient(s) more than the conventional formulation which inhibits crystallinity of the drug even on storage to maintain the drug in amorphous form to improve drug solubility, bioavailability and absorption.

This study investigated Neusilin®-based amorphous multi-component solid dispersions (NAM-SDs) containing Kollidon® VA 64 to improve aqueous solubility, bioavailability, and absorption and consequently antiplasmodial effect of lumefantrine. More so, there is a paucity of information on lumefantrine NAM-SDs in the literature.

EXPERIMENTAL

Materials

Pure sample of lumefantrine (CAS71963-77-4) was received as a gift from Hangzhou Dayangchem Co., Ltd. Neusilin® (magnesium aluminometasilicate) was a gift from Fuji Chemical, Kollidon® VA 64 was also a gift from BASF. Other chemicals and solvents employed were of analytical grade. Wistar rats were procured from the Department of Physiology, University of Nigeria, Nsukka.

Preparation of lumefantrine-loaded solid dispersions

Drug-loaded SDs were developed with Neusilin® as a carrier at different ratios utilizing the solvent evaporation process. Approximately, 80 mg of lumefantrine was fixed for all the batches at different ratios to produce second-generation (N1 - N3), third-generation (N4 - N6 and N10 - N12), and multi-component SDs (N7 - N9 and N13 - N18) at ratios 1:1, 1:2, and 1:3, respectively. Briefly, 20 mL methanol was added to a 250 mL beaker and an appropriately weighed quantity of Neusilin® (Table 1) was incorporated for each ratio and uniformly dispersed with an Ultra Turrax® homogenizer (IKA®T25DS2, Germany) at 6000 rpm for about 10 min. To the 250 mL beaker containing Neusilin dispersion, 80 mg lumefantrine, Kollidon® VA 64, and other excipients were added at the same rate. The formulations were allowed to evaporate and dry in a desiccator.

This was followed by weighing, pulverization using mortar, and then sieving (No.52). Thereafter, they were stored in airtight containers and kept in desiccators until used. Physical mixtures (N19 - N21) were prepared by mixing all the excipients and the drug in a mortar and pestle, pulverized, and sieved. Then, stored under the same condition.

Table 1: Formulation table

Sample	Drug: Neusilin®	Cr	Kr	Kv
N1	1: 1			
N2	1: 2			
N3	1: 3			
N4	1: 1	0.5		
N5	1: 2	0.5		
N6	1: 3	0.5		
N7	1: 1	0.5		1
N8	1: 2	0.5		1
N9	1: 3	0.5		1
N10	1: 1		0.5	
N11	1: 2		0.5	
N12	1: 3		0.5	
N13	1: 1		0.5	1
N14	1: 2		0.5	1
N15	1: 3		0.5	1
N16	1: 1	0.5	0.5	1
N17	1: 2	0.5	0.5	1
N18	1: 3	0.5	0.5	1
N19	1: 1	0.5	0.5	1
N20	1: 2	0.5	0.5	1
N21	1: 3	0.5	0.5	1

N1 - N3 (2nd generation SDs); N4 – N6 and N10 - N12 (3rd generation SDs); N7 – N9 and N13 - N18 (multi-component SDs); N19 – N21 (physical mix); Kv (kollidon® VA 64); Kr (kolliphor® HS 15); Cr (cremophor® RS 40).

Determination of loading efficiency

An equivalent of a unit dose of lumefantrine (80 mg) was weighed from each of the formulations into a 250 mL beaker. Then, methanolic-HCl was added and sonicated for 20 min in a sonicator (Fisher Ultrasonics, USA) and the volume made up to 100 mL. The preparation was filtered through Whatman filter paper no. 42 and 5 mL of the filtrate was collected and made up to 80 mL with methanolic-HCl. Loading efficiency was evaluated at a wavelength of 335 nm using UV spectrophotometer (Spectrumlab 752, Netherlands). Blank was prepared with methanolic-HCl. Loading efficiency (LE) was calculated using Eq 1.

$$LE\ (\%) = (RD/TD)100 \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (1)$$

Where real drug loaded (RD) is the quantity of drug encapsulated and theoretical drug loaded (TD) is the initial quantity of drug incorporated.

Flow properties of SDs

Bulk density of the SD formulations was ascertained as a ratio of the weight to the volume occupied. Tapped density was obtained as the ratio of the weight to the occupied volume of the formulation after bugging for 00 times to achieve constant volume at a height of about 2 inches from a flat surface. Then, Hausner's ratio was derived as the ratio of the tapped density to the bulk density, while the compressibility index (%) was derived as the ratio difference between the tapped density and the bulk density divided by the tapped density.

Furthermore, an earlier method was adopted in determining the flow rate and the angle of repose of the SDs using the fixed height funnel method [13]. The time it took SDs to flow via a funnel was taken and the flow rate was computed, whereas the angle of repose was calculated as an angle of Tan^{-1} of the height and radius of the SDs pile formed.

***In vitro* drug release study**

The *in vitro* release profiles of lumefantrine Neusilin®-based solid dispersions were studied using USP Type I (rotating basket) apparatus in 500 mL of phosphate buffer (PB, pH, 6.8) and simulated gastric fluid (SGF, pH, 1.2) at 100 rpm maintained at 37 ± 1 °C. An equivalent of 80 mg drug of solid dispersions, physical mix, and pure lumefantrine was encapsulated and centralized with a basket into the medium.

The basket was placed in a beaker set up on a magnetic stirrer set to rotate at 100 rpm and 37 ± 1 °C. At time intervals of 5, 10, 15, 20, 25, 30, 35, and 60 min, 5 mL aliquot of the medium was withdrawn and replaced with an equal volume of fresh medium maintained and then, diluted with methanolic-HCl and assayed at 335 nm using UV spectrophotometer (Spectrumlab, 752s, Netherlands). Determination was done in triplicate.

Characterization of SDs

Differential scanning calorimetry (DSC)

Melting transitions and changes in heat capacity of pure lumefantrine, NAM-SDs, and pure excipients were evaluated using a DSC (Netzsch DSC 204 F1, Geratebau, GmbH, Selb, Germany). Approximately 1 mg sample was weighed into an aluminum pan and the enthalpies and thermal properties were obtained at 20 - 500 ° C.

Powder diffractometry study (WAXD)

The crystalline characteristics were studied on pure lumefantrine, SDs, and physical mix using a powder diffractometer (Philips, Eindhoven, Netherlands) as previously described [14]. Prepared samples were exposed to Cu Kα radiation in the range of $0^o \leq 2\theta \leq 50^o$. The step size was 0.05º and time was maintained at 2 s.

Stability study

Physical stability of the formulation was evaluated according to International Conference of Harmonization (ICH) guidelines. Formulations were placed in air-tight containers and stored in a controlled environment at ambient temperature for about 12 months, under a spray humidifier (Bottle ORB Model 7098, Topland Co. Japan). Then, samples were removed after 12 months to determine the organoleptic properties and drug loading efficiency which was analyzed using WAXD.

In vivo antiplasmodial study

An animal experiment was conducted following the guidelines established by the Institutional Animal Care and Use Committee of the UNN, which cohered to the European community guidelines for the use of experimental animals (86/609/EEC) [15]. Wistar female mice weighing between 120 to 150 g were bred in the Department of Pharmacology and Toxicology, University of Nigeria, Nsukka. The Wistar mice were caged in good environmental conditions and kept at a body temperature of 37 °C. Before the experiment, animals were allowed free access to food and water. The chloroquine-sensitive strain of *Plasmodium berghei* NK-65 was procured from the Department of Veterinary Medicine, University of Nigeria. A 4-day suppressive test was employed for the study [16]. Approximately 0.2 mL of donor animal blood containing parasitized erythrocytes was diluted with phosphate buffer saline and was intraperitoneally inoculated into five (5) groups of six Wistar mice. Group 1 was treated with physical mix N20 (10 mg/kg), group 2 was treated with NAM-SDs, N17 (10 mg/kg), group 3 was treated with artesunate (standard, 5 mg/kg), group 4 was treated with lumefantrine (5 mg/kg), group 5 was not treated (negative control). A single oral dose per day was given. On day 4, sample blood was collected and thinly smeared on a microscope slide. Percent parasitemia was calculated and percent activity was obtained using Eq 2.

$$\text{Activity (\%)} = 100 - (ACTG/AVCG)100 \ldots\ldots \quad (2)$$

Where; AVTG is the average parasitemia of treated group while AVCG is the average parasitemia of control group.

Statistical analysis

Results were calculated and analyzed with GraphPad InStat Demo (USA) and presented as mean ± standard deviation. Variation in the means was evaluated by a two-tailed student's t-test and $p < 0.05$ was considered significant.

RESULTS

Loading efficiency of solid dispersion

Loading efficiency (LE %) of N1 – N3 (2nd generation SDs) ranged within 38.2 ± 0.28 – 40.1 ± 0.43 %, N4 - N6 and N10 – N12 (3rd generation SDs) ranged within 51.2 ± 0.46 – 67.6 ± 0.84 %, N7 – N9 and N13 - N18 (NAM-SDs) ranged within 69.3 ± 0.24 – 88.8 ± 0.86 %, while the physical mix (N19 – N21) ranged within 36.8 ± 0.37 – 47.4 ± 0.80 %. There was a significant reduction in LE (%) of NAM-SDs (multicomponent SDs containing Kolliphon® VA 64) compared to other formulations ($p < 0.05$).

Flow property

Bulk and tapped densities of all the batches ranged within 0.42 ± 0.6 - 0.44 ± 0.4 and 0.50 ± 0.44 - 0.54 ± 0.44 (g/mL), while the physical mix ranged within 0.50 ± 0.3 - 0.52 ± 0.3 and 0.64 ± 0.24 - 0.67 ± 0.5 (g/mL), respectively. All the formulations had Hausner's ratio < 1.25 except the physical mix that fell within 1.28 - 1.30. Angle of repose ranged between 39 ± 0.4° and 46 ± 1.1° for formulations N7 - N9 and N13 - N21 (NAM-SDs) except formulations N1 - N6 and N10 - N12 (2nd and 3rd generations SDs) that ranged within 20 ± 0.9° and 25 ± 0.4°, respectively. While the flow rate ranged between 6.5 ± 0.14 to 7.5 ± .32 g/s for formulations N1 - N6 and N10 - N12 and 1.1 ± 0.41 to 1.9 ± 0.27 g/s for formulations N7 - N9 and N13 - N21.

In vitro release study

Time to release 45 % ($T_{45\%}$) and 60 % ($T_{60\%}$) of the drug in pH, 6.8 for formulations N17 and N20, and pure drug were 15, 10, and 0 min, and 20, 45, and 0 min, respectively. In the SGF (pH, 1.2) T_{45} showed 15, 55, and 0 min, while T_{60} includes 50, 0, and 0 min for formulations N17, N20, and pure drug, respectively (Figure 1).

Characterization of solid dispersions

Lumefantrine thermogram showed a very sharp endothermic peak at 133.4 °C with a transition enthalpy of -7.584 mW/mg (Figure 2 A). The broad curve of Neusilin® indicated a high amorphous curve of the polymer, while other excipients Cremophor® RH 40, Kollidon® VA 64, and Kolliphor® HS 15 showed broad thermogram peaks at 84.3, 74.1, and 65.6 °C respectively.

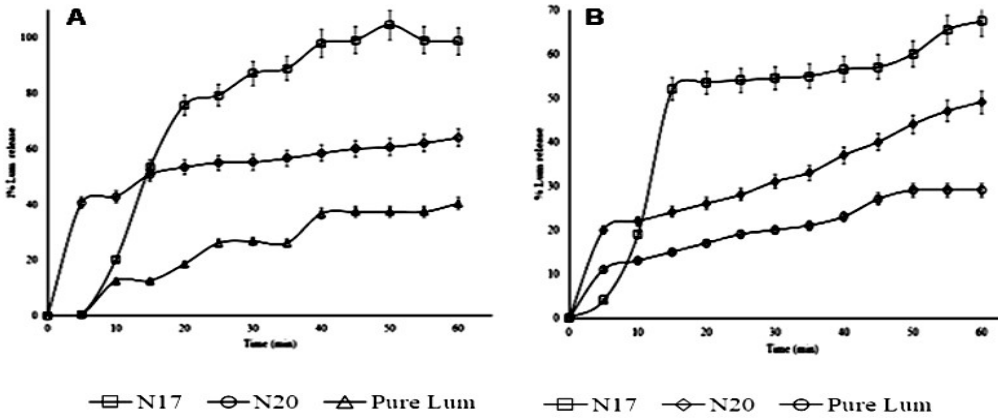

Figure 1: Drug release of lumefantrine from Neusilin® solid dispersion in (A) phosphate buffer (pH, 6.8) and (B) SGF (pH, 1.2). ***Key:*** N17 (NAM-SDs), N20 (physical mix), pure lum (pure lumefantrine sample)

Table 2: Loading efficiency and flow properties of solid dispersions (mean ± SD)

Batch	BD (g/mL)	TD (g/mL)	A (º)	LE (%)	*LE (%)
N1	0.469±0.2	0.500±0.87	20±1.2	39.9±0.32	35.8±0.22
N2	0.441±0.4	0.509±0.45	22±0.8	40.1±0.43	37. 2±0.12
N3	0.484±0.6	0.517±0.32	20±0.6	38.2±0.28	33.0±0.18
N4	0.429±0.3	0.506±0.49	23±0.4	51.2±0.46	48.7±0.40
N5	0.441±0.4	0.510±0.46	24±0.7	57.4±0.34	55.9±0.11
N6	0.429±0.3	0.500±0.32	24±0.4	55.6±0.38	54.0±0.20
N7	0.417±0.6	0.500±0.44	42±0.6	69.3±0.24	68.7±0.44
N8	0.441±0.1	0.500±0.45	44±0.7	78.6±0.80	78.2±0.12
N9	0.429±0.3	0.536±0.43	46±0.8	75.0±0.46	74.8±0.51
N10	0.441±0.8	0.509±1.20	25±0.4	55.8±0.35	51.7±0.15
N11	0.429±0.5	0.507±0.94	24±0.6	67.6±0.84	62.2±0. 33
N12	0.441±0.4	0.500±0.32	24±0.7	52.5±0.32	49.6±0.19
N13	0.429±0.6	0.536±0.46	42±0.8	75.9±0.36	75.8±0.30
N14	0.441±0.3	0.500±0.33	46±0.9	76.8±0.49	76.8±0. 23
N15	0.429±0.2	0.536±0.41	46±0.5	75.9±0.38	75.7±0.75
N16	0.417±0.4	0.517±0.24	40±0.7	69.5±1.20	69.1±0.11
N17	0.441±0.1	0.536±0.44	39±0.4	88.8±0.86	88.1±0.53
N18	0.429±0.5	0.536±0.31	42±0.6	76.8±0.46	76.5±0.42
N19	0.500±0.2	0.641±0.24	42±0.7	36.9±0.34	30.9±0.16
N20	0.517±0.3	0.667±0.47	44±0.3	47.4±0.80	33.5±0.20
N21	0.500±0.4	0.654±1.50	40±1.2	36.8±0.37	30.1±0.44

Note: N1 - N3 (2nd generation SDs), N4 – N6 and N10 - N12 (3rd generation SDs), N7 – N9 and N13 - N18 (NAM-SDs), N19 – N21 (physical mix), LE (loading efficiency after formulation), *LE (loading efficiency after 12 months), SD (standard deviation), A (angle of repose), BD and TD (bulk and tapped densities, respectively).

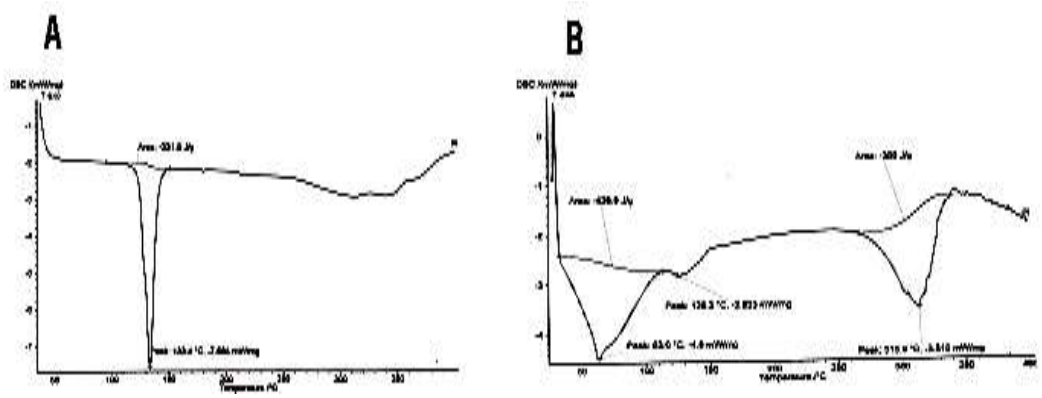

Figure 2: DSC thermograms of (A) lumefantrine and (B) solid dispersions (NAM-SDs)

Formulation N17 (NAM-SDs) thermogram indicated a broader transition thermogram at 63.0 °C with an accompanying enthalpy of -4.5 mW/mg (Figure 2 B).

Wide-angle X-ray diffraction (WAXD)

The diffractogram of the pure lumefantrine depicted a crystalline state with a sharp peak at 2Θ > 5° and high intensity (Figure 3). The SDs formulations containing a single surfactant (N11, Kolliphor® HS 15) or (N5, Cremophor® RH40) showed a higher peak intensity than formulations N17 (NAM-SDs) and N20 (physical mix) with Kollidon® VA 64 (a crystalline inhibitor).

Stability study

There was no change in organoleptic properties of the formulations after the test. Also, there was no significant difference in the loading efficiency of 2nd generations SD formulations after 12 months unlike in the NAM-SD formulations. The WAXD showed that NAM-SDs maintained a sharp peak of lumefantrine at 2Θ > 5° with high intensity.

In vivo antiplasmodial study

Percent antiplasmodial activity ranged from 90 – 98, 60 – 80, 65 – 81 and 20 - 45 % for formulations NAM-SDs (N17), N20, artesunate tablet, and pure lumefantrine, respectively. The highest anti-plasmodial activity was observed in NAM-SDs (Figure 4).

DISCUSSION

Neusilin amorphous multi-component SDs (NAM-SDs) containing Kollidon VA 64 were produced to show amorphous properties as revealed by the DSC and WAXD characteristics.

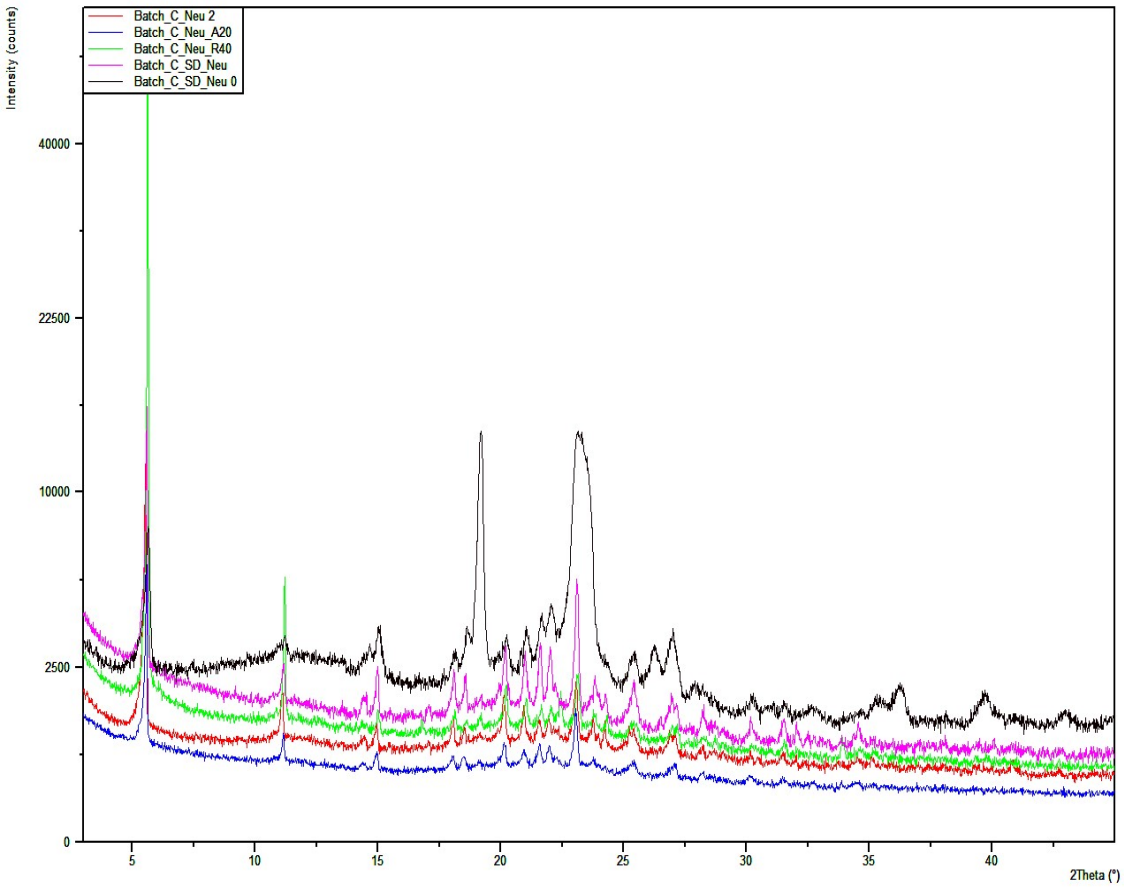

Figure 3: Composite WAXD of lumefantrine and NAM-SDs formulations. ***Key:*** Batch C Neu 2 (N20, containing lumefantrine + Neusilin® + kolliphor HS 15 + Cremorphor® RH40 + Kollidon® VA 64), batch C Neu A20 (N17, containing lumefantrine + Neusilin® + kolliphor HS 15 + Cremophor® RH40 + Kollidon® VA 64), batch C Neu RH40 (N5, containing lumefantrine + Neusilin® + cremophor® RH40), batch C SD Neu (N11, containing lumefantrine + Neusilin + kolliphor HS 15); Batch C SD Neu 0 (lumefantrine)

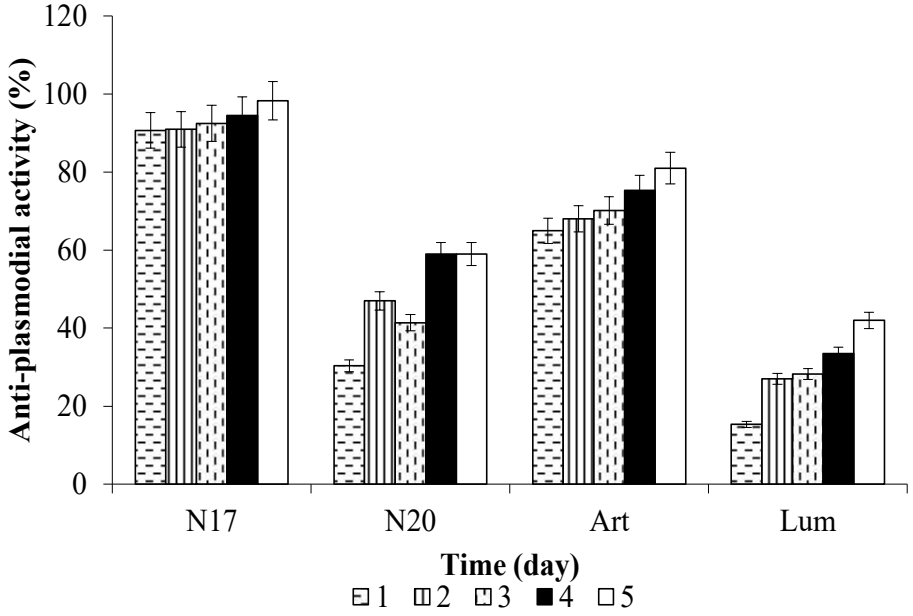

Figure 4: An *in vivo* antiplasmodial study. ***Key:*** N17 (NAM-SDs); N20 (physical mix), Art (artesunate); Lum (lumefantrine)

The NAM-SDs showed a decreased flow property. Meanwhile, it exhibited the highest *in vitro* (drug release) and *in vivo* (antiplasmodial) activities, unlike other generation SDs. The NAM-SDs exhibited the highest drug loading due to the generated fewer perfect crystals with more imperfections, which caused more drug entrapment and localization. More so, the discrepancy observed in LE (%) of NAM-SDs and other SDs-generations may be a result of the impact of Kollidon® VA 64, a copolymer with crystal inhibition effect. This incorporated polymer enhanced lumefantrine solubility. A previous report showed that the lipophilicity of the drug, type of components, combination ratios of the components, and formulation technique may affect loading efficiency [17]. Decrease in flowability of the NAM-SDs might be due to the presence of Kollidon VA 64 which exhibits plasticity (increased mostly on exposure to atmospheric temperature). The highest drug release of NAM-SDs (N17) in SGF (pH, 1.2) indicated an improved solubilization property with fewer or no crystal formation. This effect may be a result of the presence of Kollidon® VA 64 (crystal inhibitor) and Neusilin® which imparted amorphous properties to the SDs. The dissolution rate improvement by Kollidon VA 64 is established on the carrier's solubilization rule to generate a hydrotropic condition for PWSDs. The improvement in drug release may be due to the presence of drugs/excipients in the microenvironment. The Kollidon® VA 64 being a copolymer dissolved rapidly on contact with the dissolution medium due to the presence of a pyrrolidone ring which has very good solubility in an aqueous medium.

The presence of vinyl acetate in Kollidon® VA 64 might have caused a decrease in the glass transition temperature (Tg) of the SDs and lowered hygroscopicity. This is consistent with an earlier report [18]. The broader thermogram suggested molecular dispersion of the drug was in the multi-component matrix, transforming from a crystalline state to an amorphous state. The transition from crystalline to amorphous state may perhaps cause an encapsulated drug to be retained over a while [19,20]. This amorphous nature also indicated the generation of more spaces for drug localization. Amorphous state depicted a disarrayed structure with a pushing force (thermodynamic). This leads to greater aqueous solubility, loading efficiency, release, absorption, and bioavailability due to the numerous pores created [20,3]. The obtained higher solubility of amorphous substances is a result of a higher enthalpy, entropy, free energy, and volume compared to the crystalline substance [17].

Diffractograms of NAM-SDs generally showed a decrease in the melting peak intensities indicating a decrease in the crystalline nature of lumefantrine produced in a higher amorphous matrix. This depicted that third-generation formulations (N11 and N5) would exhibit better stability since an increase in crystallinity increases purity and stability, while the NAM-SDs (N17) and the physical blend of (N20) were amorphous. The higher amorphous nature observed in NAM-SDs (containing Kollidon® VA 64) created higher spaces within the SDs for lumefantrine entrapment to enhance the physicochemical properties of the drug. This agrees with an earlier report [19]. The high antiplasmodial property of the formulation NAM-SDs (N17) may be due to the amorphous formulation produced which achieved higher wettability, solubilization, dissolution, and then higher *in vivo* drug absorption.

CONCLUSION

Neusilin®-based amorphous multicomponent solid dispersions (NAM-SDs) enhance the aqueous solubility, bioavailability and absorption of lumefantrine. The NAM-SDs containing Kollidon® VA 64 generate amorphous SDs with higher antiplasmodial activity. The amorphous state exhibits depicted a disarrayed structure with greater thermodynamic force leading to improved physicochemical characteristics and bioavailability compared to other SD generations. The DSC and WAXD show more solubilized and less crystallinity (higher amorphous state) of NAM-SDs indicating more pores for drug entrapment and localization. Hence, lumefantrine Neusilin® based amorphous multicomponent solid dispersions is a potential drug delivery carrier to improve the stability, solubility, and bioavailability of the drug.

DECLARATIONS

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Ethical approval

None provided.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflict of Interest

No conflict of interest associated with this work.

Contribution of Authors

We declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by the authors. Prof Ikechukwu V. Onyishi proposed and supervised this work, Dr. CE. Ugwu carried out the experimental work, Dr. EO Diovu and BC Obitte did the write-up, while Prof GC. Onunkwo, Prof IV Onyishi, and Prof MA Momoh read and approved the manuscript.

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REFERENCES

1. *Ugwu CE, Agubata CO, Chime SA, Obitte NC, Onyishi IV, Onunkwo GC, Ofoefule SI, Chukwu A. Development of a modified hard gelatin capsule for colon-targeted drug delivery of hydrogel-based piroxicam microparticles. Trop J Pharm Res 2022; 21(11): 2285-2293.*
2. *Janssens S, Van Den Mooter G. Review: physical chemistry of solid dispersions. J Pharm Pharmacol 2009; 61: 1571-1586.*
3. *Jain S, Patel N, Lin S. Solubility and dissolution enhancement strategies: Current understanding and recent trends. Drug Dev Ind Pharm 2015; 41: 875-887.*
4. *Ugwu CE, Ugwu DC, Attama AA. Formulation and in vitro characterization of amorphous-based solid dispersion of an antimalarial drug. Int J Pharm Sci Rev Res 2019; 58(2): 1-9.*
5. *Kumar S, Satish K Gupta. Pharmaceutical solid dispersion technology: A strategy to improve the dissolution of poorly water-soluble drugs. Recent Pat Drug Del Forrmul 2013; 7: 2.*

6. Sridhar I, Doshi A, Joshi B, Wankhede V, Doshi J. Solid Dispersions: An approach to enhance the solubility of the poorly water-soluble drug. J Scient Innov Res 2013; 2(3): 685-694.
7. Verma S, Rawat A, Kaul M, Saini S. Solid Dispersion: A strategy for solubility enhancement. Int J Pharm Tech 2011; 3(2): 1062-1099.
8. Chiou WL, Riegelman S. Pharmaceutical application of solid dispersion system. J Pharm SC 1971; 60(9): 1281-1302.
9. Yan YD, Sung JH, Kim KK, Kim DW, Kim JO, Lee BJ. Novel valsartan-loaded solid dispersion with enhanced bioavailability and no crystalline changes. Int J Pharm 2012; 422: 202-210.
10. Saffoon N, Uddin R, Huda NH, Sutradhar KB. Enhancement of oral bioavailability and solid dispersion: A Review. J Appl Pharm Sci 2011; 1(07): 13-20.
11. Rao AB, Shivalingam MR, Reddy K, Rao S, Rajesh K, Sunitha N, Formulation and evaluation of aceclofenac solid dispersions for dissolution rate enhancement. Int J Pharm Sci Drug Res 2010; 2(2): 146-150.
12. White NJ, Lallo D, Kang G, Junghanss, Hotez P, Garcia P, Farrar J. Manson's Tropical Diseases. Elsevier 2024. p. 1- 10.
13. McKenna A, McCafferty DF. Effect of particle size on the compaction mechanism and tensile strength of tablets. J Pharm Pharmacol 1982; 34: 347-351.
14. Momoh AM, Ugwu EC, Nafiu A, Kenechukwu CF, Adedokun OM, Usman M, Barikisu A, Oyeniyi YJ, Ofokansi KC, Attama AA, et al. Mucin-grafted polyethylene glycol microparticles enable oral insulin delivery for improving diabetic treatment. Appl Sci 2020; 10: 2649
15. European Community Council Directive on the ethics of experiments involving laboratory animals (86/609/EEC), November 24 (1986).
16. Peters W, Robinson BL. The chemotherapy of rodent malaria. Annals of Trop Med Parasitol 1993; 87: 111-123.
17. Kenechukwu FC, Attama AA, Ibezim EC, Nnamani PO, Umeyor CE, Uronnachi EM, Gugu TH, Momoh MA, Ofokansi KC, Akpa PA. Surface-modified mucoadhesive microgels as a controlled release system for miconazole nitrate to improve localized treatment of vulvovaginal candidiasis. Eur J Pharm Sci 2018; 111: 358–375
18. Fule R, Meer T, Sav A, Amin P. Solubility and dissolution rate enhancement of lumefantrine using hot melt extrusion technology with physicochemical characterization. J Pharmaceut Invest 2013; 43: 305–321.
19. Attama AA, Muller-Goymann CC. A critical study of novel physically structured lipid matrices composed of a homolipid from Capra hircus and theobroma oil. Int J Pharm 2006; 322: 67–78.
20. Agubata CO, Nzekwe TI, Attama AA, Mueller-Goymann CC, Onunkwo GC. Formulation, characterization, and anti-malarial activity of homolipid-based artemether microparticles. Int J Pharma 2015; 478: 202-222.