

# Enhancement of dissolution of *Prosopis africana* stem bark extract by solid dispersion technique

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## ABSTRACT

**Background and Aims:** Literature reveals many benefits and potentials of the stem bark extract of *Prosopis africana* but like other plant extracts, its use in the oral pharmaceutical formulation is limited due to its poor aqueous solubility, reduced absorption, and bioavailability. The aim of this study is to develop oral solid dispersion formulations of *Prosopis africana* extract to improve its dissolution and possible bioavailability.

**Methods:** Crushed stem bark of *Prosopis africana* was macerated in methanol for 72 h at room temperature. The resulting extract (PREx) was incorporated into polyethylene glycol 4000 (PEG 4000) by the solvent-evaporation and melt-fusion methods using different ratios (1:1, 1:2, 1:4) of extract to polymer; physical mixtures of the same ratio of extract to polymer were also prepared. The crystallinity of the formulations was characterized by differential scanning calorimetry (DSC), possible interaction/incompatibility between the extract and polymer was determined by Fourier transform infra-red spectroscopy (FT-IR). *In vitro*, release and modeling of the release profile were also determined.

**Results:** No interaction was found between materials used for the preparations while DSC thermograms showed a reduction in crystallinity of PREx in the solid dispersion formulations. *In vitro* release profile of the formulation prepared with the highest polymer concentration by the melt-fusion method (M3) showed the greatest enhancement in dissolution.

**Conclusion:** This study shows solid dispersion prepared by the melt-fusion method as an effective technique for the enhancement of dissolution of poorly water-soluble *Prosopis africana* extract.

**Keywords:** Melt-fusion, *Prosopis africana* extract, PEG 4000, solid dispersion

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## INTRODUCTION

The use of medicinal plants is as old as mankind in the treatment of various diseases. Parts of plants such as roots, leaves, fruits, buds, stems, flowers, and barks contain biochemically active constituents which are thought to be responsible for the cure and management of various diseases.

In African nations, the utilization of these plants as the primary source of or an integral part of healthcare is well-documented (WHO, 2004; Bandaranayake, 2006; Sofowora, Ogunbodede, & Onayade et al., 2013). This is understandable because in developing climes like Africa, with high poverty rates, access to and affordability of the usual conventional drugs is a challenge. Moreover, herbal medicines are believed to be readily accepted due to their purported claim of relative safety.

Although plant extracts are considered to have remarkable *in vitro* properties, the *in vivo* efficacy is usually limited due to low aqueous solubility resulting in reduced absorption and bioavailability (Gunasekaran, Haile, Nigusse, & Dhanaraju, 2014; Nikam, Shete, & Khapare, 2020). To address such solubility problems, formulation with suitable polymers has proved positive (Ansari & Parveen, 2016).

Solid dispersion is a technique of dispersing one or more active hydrophobic ingredients in an inert hydrophilic carrier or matrix in a solid state resulting in improved solubility and better bioavailability (Nikam et al., 2020; Enose, Dasan, Sivaramakrishnan, & Shah, 2014). This technique converts the crystalline form of drugs into the amorphous form which enhances its bioavailability and improves its dissolution kinetics (Wani et al., 2021). When solid dispersion formulations come in contact with aqueous media, the carrier dissolves and the drug is released as very fine colloidal particles or oily globules of sub-micron sizes.

The solid dispersion technique is beneficial in overcoming the solubility, dissolution, and bioavailability complications of poorly soluble phytoconstituents. These can be achieved by optimizing the surface area available for dissolution through the reduction of particle size of the solid compound and/or by enhancing the wetting characteristics of the drug compound surface, to decrease the boundary layer thickness and ensure sink conditions for dissolution (Sharma, Sahoo, Agrawal, & Kumari, 2019; Rahman, 2020; Singh, Baghel, & Yadav, 2021). Apart from improving the dissolution of poorly soluble phytoconstituents, the solid dispersion technique has been used to mask disagreeable tastes, odor, and smell and in reducing gastric irritation (Cai et al., 2014; Qusa, Siddique, Nazzal, & El Sayed, 2019). In addition, the technique has been exploited to control the release of phytoconstituents (Cid, Simonazzi, Palma, & Bermúdez, 2019), protect phytoconstituents from degradation, and improve constituent's stability (Parikh, Kathawala, Song, Zhou, & Garg, 2018; Saidan, Kaus, Aisha, Hamil, & Ismail, 2020) while also reducing therapeutic dose and possible side effects (Rahman, 2020).

Methods used in the preparation of solid dispersions include solvent evaporation which involves the dissolution of the drug

and carrier in a suitable solvent. Evaporation of the solvent leaves a film or mass which can be dried to constant weight. Another method is the melt method which involves heating the drug and suitable carrier at temperatures above their eutectic points until both are melted. The melted mixture is rapidly cooled to obtain a congealed mass which can be pulverized and sieved (Kumar & Kumar, 2017). Other methods include co-precipitation, kneading, co-grinding, gel entrapment, spray-drying, and freeze drying.

Literature reveals reports of studies on the formulation of poorly water-soluble herbal constituents and/or, extracts by solid dispersion techniques. The study by Onoue et al., (2010) showed that the pharmacokinetic behavior and photo-stability of curcumin were significantly enhanced when prepared as a solid dispersion. Another study reported increased solubility of quercetin in solid dispersion formulations (Costa et al., 2011). The hepatic activity of poorly water-soluble silymarin was observed to increase when developed as solid dispersion (Balata & Shamrool, 2014). In a different study, a solid dispersion formulation of fat-soluble *Ginkgo biloba* extract significantly improved its dissolution (Wu et al., 2018). In another study, solid dispersion formulation of the ethanol extract of *Andrographis paniculata* enhanced its solubility, furthermore, compression of the solid dispersion into tablets showed enhanced dissolution and oral bioavailability of the extract (Nitave, Chougule, & Koumaravelou, 2018).

In a different study, alginate encapsulation of turmeric extract solid dispersions showed stronger antibacterial activity than other formulations of the extract (Bangun, Arianto, Bangun, & Nainggolan, 2019). Formulation of solid dispersion of *Fagonia indica* extract showed significant anti-hepatotoxicity activity and complete recovery from hepatotoxicity when compared to the crude extract alone (Shehab, Shahiwala, Benouared, & Khan, 2020). The study by Tafu & Jideani, (2021) suggested that solid dispersions of the popular *Moringa oleifera* leaf powder may be useful in functional foods and beverages and in nutraceutical formulations. Bajracharya, Song, Lee, Jeong, & Han, (2022) reported that solid dispersion of *Isatis indigotica* and *Juglans mandshurica* produced better dissolution and oral absorption of the combined extract than when used in their crude form.

*Prosopis africana* (*P. africana*) is the only tropical African *Prosopis* species, and belongs to the family Fabaceae, sub-family *Mimosoideae*. It is a leguminous tree native to Africa and Asia and is found abundantly in the middle belt regions of Nigeria. It is popularly called the Locust beans tree, or Ironwood tree and in Nigeria, it is known as "kiriya" by the Hausas, "okpehe" by the Idoma, "ubwa" by the Igbos and "ayan" by the Yorubas (Bello, Madusolumuo, & Igbokwe, 2016; Odoh et al., 2018).

Different parts of the tree have been used for the management of ailments ranging from toothache, sore throat, bronchitis, dysentery, gonorrhoea, dermatitis, and skin diseases to malaria (Kolapo, Okunade, Adejumbi, & Ogundiya, 2009; Nnamani, Kenechukwu, Chika, & Otuu, 2012). Specifically, the fresh leaf buds and shoots have been used as fodder while the pods are consumed by cattle as well as been a rich source of potash

for the manufacture of local soap (Orwa, Mutua, Kindt, Jamnadass, & Anthony, 2009; Ajiboye, Agboola, Fadimu, & Afolabi, 2013). In the middle belt states of Nigeria, the fermented seeds of the plant are popularly used as a food seasoning; other parts are used in the preparation of soups and the making of cakes (Achi & Okolo, 2004). Laboratory investigations have confirmed that the extract possesses anti-inflammatory, antidiabetic, antibacterial, antifungal, anti-ulcer, anticancer, and anthelmintic properties among others (Okide, Odoh, & Ezugwu, 2003; Atawodi & Ogunbusola, 2009; Ayanwuyi, Yaro, & Abodunde, 2010; Ibrahim, Mohammad, Faisal, & Musa, 2018; Alimata et al., 2020).

In spite of the potential of *Prosopis africana* extract, its use in the pharmaceutical formulation is limited due to its poor aqueous solubility, reduced absorption, and bioavailability as with other plant extracts (Rohini, Muhammad, & Rabeta, 2021). Therefore, the aim of this work is to develop solid dispersion formulations of the methanol stem bark extract of *Prosopis africana* using a hydrophilic polymer (polyethylene glycol; PEG 4000). The novelty of this work is in the development of a solid dispersion formulation containing the methanol stem bark extract of *Prosopis africana* which has not been hitherto reported.

## MATERIALS AND METHODS

### Materials

Methanol extract of *Prosopis africana* stem bark, polyethylene glycol 4000 (Merck, Germany), methanol (Sigma, Aldrich, United Kingdom), and hydrochloric acid (Sigma Aldrich, United Kingdom).

### Collection and preparation of plant material

The stem bark of *Prosopis africana* was deposited at the botanical garden of the National Institute for Pharmaceutical Research and Development (NIPRD), Abuja, Nigeria, and given the voucher number; NIPRD/H/7285. The dried stem barks were cleaned, air-dried, and pulverized using a mechanical grinder. The coarse powder obtained was packaged in an air-tight container and stored in a desiccator until further use.

### Preparation of the extract of *Prosopis africana*

An earlier method was adopted with some modifications (Ayanwuyi et al., 2010). About 1 kg of the pulverized powdered stem bark was macerated in 70% methanol (v/v) in a ratio of 1:3 (powdered stem bark: methanol) for 72 h at room temperature with intermittent stirring. After soaking, the mixture was filtered using a muslin cloth. The extract was concentrated over a water bath (Karl Kolb, Germany) at 70 °C and the resulting extract (PREX) was pulverized and stored in an air-tight container until further use.

### Preparation of solid dispersion formulations

#### Solvent evaporation method

Three (3) different batches of solid dispersion formulations were prepared using polyethylene glycol (PEG) 4000 at extract: polymer ratios of 1:1, 1:2, and 1:4 using methanol as the solvent of choice. Appropriate amounts of the extract (PREX) and polymer (PEG 4000) as displayed in Table 1 were used. The extract (2.5 g) and polymer (2.5 g) were mixed, placed in a beaker, and dissolved with sufficient volume (20 mL) of methanol

with continuous stirring. The solvent was completely evaporated over a water bath at 40 °C while continuously stirring to obtain a dried mass. The dried mass was pulverized, screened through a sieve (A.S.T.M. E-11 Specification No. 60), packaged in an air-tight container, and coded as S1; this was stored in the desiccator until further use. The other batches were prepared similarly using 2.5 g of extract and 5 g of polymer for batch S2 and 2.5 g of extract and 10 g of polymer for batch S3 (Table 1).

**Table 1. Composition of solid dispersion batches.**

Batch	PREx (g)	PEG 4000 (g)
S1	2.5	2.5
S2	2.5	5
S3	2.5	10
M1	2.5	2.5
M2	2.5	5
M3	2.5	10
P1	2.5	2.5
P2	2.5	5
P3	2.5	10

### Melt fusion method

Three (3) different batches of solid dispersion formulations were prepared using polyethylene glycol 4000 (PEG 4000) at extract:polymer ratios of 1:1, 1:2, and 1:4 using the melt-fusion method. As displayed in Table 1, 2.5 g of extract and 2.5 g polymer (PEG 4000) were mixed together, placed in a beaker, and heated directly on the hot plate at 50 - 55 °C while stirring at 50 rpm (until melted). The molten mixture was continuously stirred until the extract was completely melted into a homogeneous mass. The melted mass was rapidly cooled on an ice pack under vigorous stirring. The solid mass was crushed, pulverized, and sieved through a sieve (A.S.T.M. E-11 Specification No. 60), packaged in an air-tight container, and labeled as M1, this was stored in the desiccator until further use. The other batches were prepared similarly according to the composition in Table 1 and coded M2 and M3.

### Physical mixture method

Physical mixtures were prepared by manually mixing appropriate amounts of the extract and PEG 4000 according to the composition in Table 1. The extract (2.5 g) was mixed with 2.5 g of PEG 4000 in a porcelain mortar for about 3 min, the powdered mixture was packaged in an air-tight container and labeled P1. Batches P2 and P3 were prepared in the same manner using the appropriate quantities as stated in Table 1, packaged appropriately, and stored in the desiccator until further use.

### Evaluation of solid dispersion formulations

#### Determination of product yield

The product yield of each batch was determined by the ratio of the weight of the dried dispersions and the sum of the starting materials (using amounts of PREx and PEG 4000 as displayed in Table 1) expressed in percentage.

### Fourier transform-infrared (FT-IR) spectra studies

The solid dispersions were triturated with potassium bromide, made into pellets (1 ton/cm<sup>2</sup>) and infrared (IR) spectra were obtained between scanning ranges of 4000 and 400cm<sup>-1</sup> using the Cary 630 Fourier transform infrared (FT-IR) Spectrometer (Agilent Technologies, USA).

### Differential scanning calorimetry (DSC) analysis

Samples of the optimized solid dispersion formulations; M3, PM3, and the extract alone (4.7 - 6.3 mg) were placed in aluminum pans of the differential scanning calorimetry (DSC) (Model DSC 204 F1Netzsch, Germany). The pans were crimped and heated between 60 and 300 °C at a scanning rate of 10 °C/min under constant nitrogen flow at a rate of 20 mL/min.

### In vitro dissolution studies

The calibration curve of the extract (PREx) was prepared using concentrations of 40-100 µg; scans of the extract and their corresponding absorbance were obtained from the UV-Visible spectrophotometer (Cary 60). *In vitro*, dissolution was conducted the United States Pharmacopeia (USP) apparatus II (paddle method) at a speed of 100 rpm. An amount of the solid dispersion formulation (50 mg) was placed in the dissolution vessel containing 0.1N Hydrochloric acid, maintained at 37 ± 0.5 °C. The dissolution test was carried out for 60 min, and aliquots of 5 mL were withdrawn from the vessels at predetermined intervals of 5, 15, 30, 45, and 60 min, and the same volume of medium was replaced into the vessel to maintain sink condition. The same procedure was repeated for all the other solid dispersion formulations and the extract alone. The absorbance of the withdrawn samples was determined using the Ultra-violet (UV)-Visible spectrophotometer (Cary 60) at 230 nm, and the content of PREx was determined from the calibration curve.

### Modeling of release profile

The kinetics of extract release was determined by fitting the data obtained from *in vitro* release studies into the zero-order, first-order, Higuchi, and Hixson-Crowell models while the mechanism of release was determined by the Korsmeyer-Peppas model. The model with the highest coefficient value was selected as the appropriate model used to describe the possible kinetics and mechanism of the extract's release from the solid dispersion formulations. The equations that describe the model-dependent mathematical kinetics are as follows:

$$\text{Zero order} = Q_t = Q_0 + K_0 t \quad \text{Eq 1}$$

$$\text{First order} = \ln Q_t = \ln Q_0 + K_1 t \quad \text{Eq 2}$$

$$\text{Higuchi} = Q_t = K_h t^{1/2} \quad \text{Eq 3}$$

$$\text{Hixson-Crowell} = Q_0^{1/3} + Q_t^{1/3} = K_d t \quad \text{Eq 4}$$

$$\text{Korsmeyer-Peppas} = Q_t/Q_\infty = K_{kp} t^n \quad \text{Eq 5}$$

where  $Q_t$  is the drug dissolved amount in time  $t$ ,  $Q_0$  is the initial quantity of drug in the solution,  $K_0$  is the zero-order release constant,  $K_1$  is the first-order release constant,  $K_h$  is the Higuchi rate constant,  $K_d$  is the dissolution constant of Hixson-Crowell kinetics,  $Q_t/Q_\infty$  is a proportion of drug released at time  $t$ ,  $K_{kp}$  is the Korsmeyer-Peppas release rate constant.

## RESULTS

### Determination of product yield

Product yield for all the formulations was between 65.32 and 92.97 % with physical mixture formulations having the highest yield and solvent evaporation method having the least yield (Table 2).

**Table 2. Product yield of solid dispersion formulations and physical mixture.**

Formulation	Yield (%)
S1	65.32
S2	78.52
S3	81.69
M1	90.24
M2	76.80
M3	88.70
P1	84.12
P2	92.97
P3	83.96

### Fourier transform-infrared (FT-IR) spectroscopy analysis

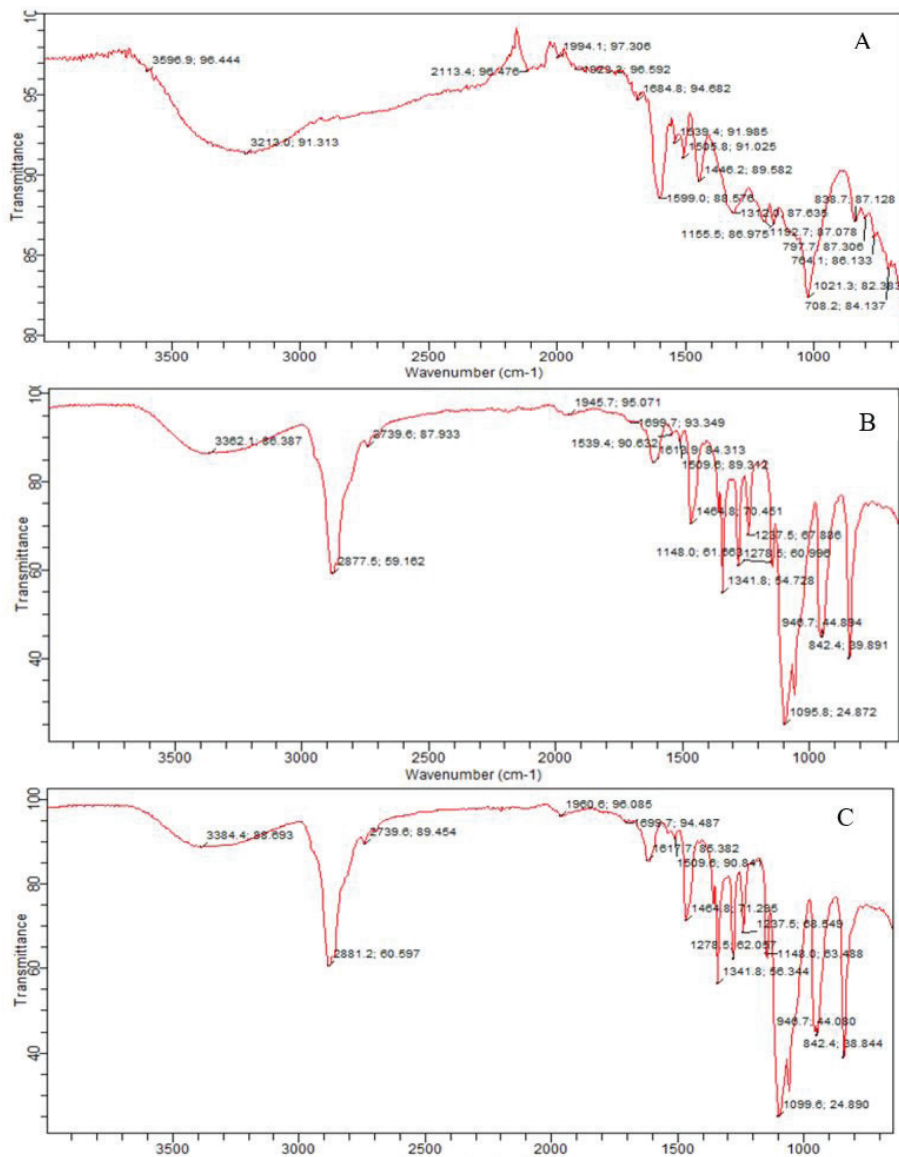
FT-IR spectroscopy analysis was carried out to investigate any physicochemical interactions between the crude extract (PREx) and the polymer used in the preparation of the solid dispersions. The spectra for PREx, the optimized batch for the physical mixture (P3), and solid dispersion prepared by the melt-fusion method (M3) are displayed in Figures 1A, 1B, and 1C respectively.

Characteristic peaks of PREx were observed at 3596.9cm<sup>-1</sup>, 2113.4, 1599.0, 1312.0 cm<sup>-1</sup>, 1021.3, and 708.2cm<sup>-1</sup> (Figure 1A). The IR spectrum of the physical mixture (Figure 1B) and solid dispersion (Figure 1C) were observed to be similar. However, the peak at 2113.4cm<sup>-1</sup> due to the extract was observed to be smoothed in the presence of the polymer (Figures 1B and 1C).

### Differential scanning calorimetry (DSC) analysis

Differential scanning calorimetry (DSC) is a thermal analysis technique in which the heat flow into or out of a sample is measured as a function of temperature or time. Figure 2A shows the DSC thermogram of the pure extract (PREx), the optimized physical mixture (Figure 2B), and the optimized solid dispersion prepared by the melt-fusion method (Figure 2C). PREx showed an endothermic peak beginning at 59.99 °C and ending at 299.96 °C with a peak temperature of 177.74 °C corresponding to its crystalline melting peak as displayed in Table 3.

Thermal properties of the physical mixture and solid dispersion formulation were observed to differ from those of the crude extract (PREx). The endothermic melting peak of the extract was observed to be broadened in Figure 2B and completely absent in Figure 2C. Change in heat of enthalpy of PREx (779.45 J/g) displayed in Table 3 is seen to decrease in P3 (692.00 J/g) and considerably decreased in M3 (614.92 J/g).



**Figure 1.** FT-IR spectra of PREx (A), physical mixture of PREx and PEG 4000 (B), solid dispersion of PREx and PEG 4000 prepared by melt-fusion (C).

**Table 3. Thermal properties of PREx and solid dispersion formulations.**

Parameter	PREx	P3	M3
Onset temperature (°C)	59.99	61.53	34.26
Peak temperature (°C)	177.74	86.07	75.88
Conclusion temperature (°C)	299.96	101.11	228.74
Enthalpy of crystallization (J/g)	779.45	692.00	614.92
Crystalline melting temperature range; ΔT (°C)	239.97	39.58	194.48

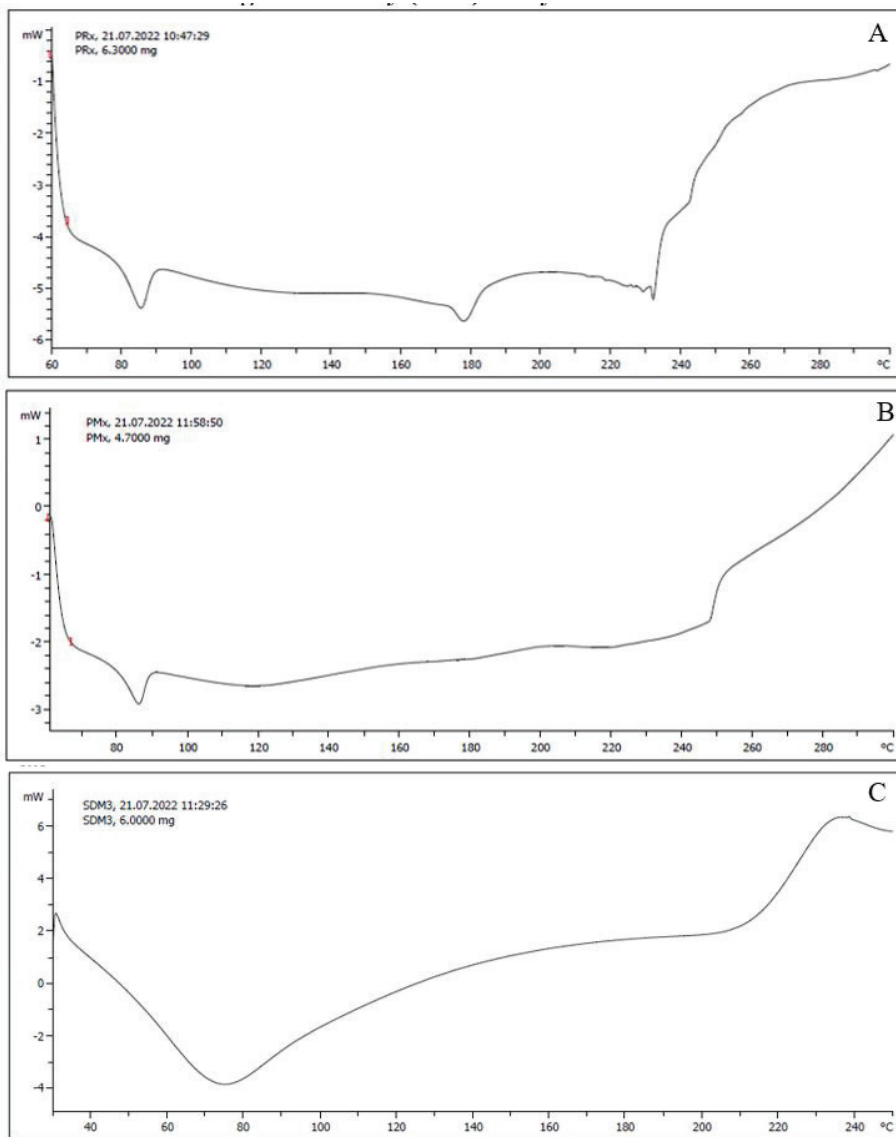
**In vitro dissolution studies**

Results of *in vitro* dissolution studies for the solid dispersion formulations prepared by the solvent-evaporation, melt-fusion method, physical mixture, and crude extract alone (PREx) are presented in Figure 3. Extract release from the formulations

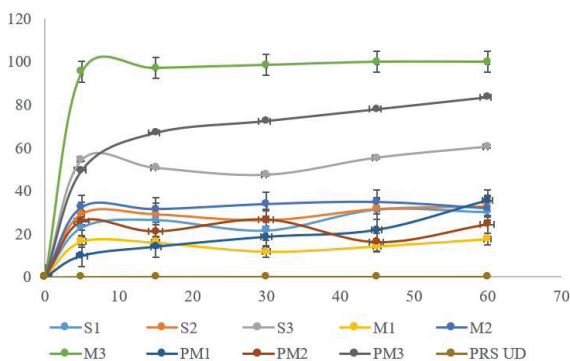
was observed to be polymer concentration-dependent irrespective of the method of preparation. However, the melt-fusion formulations showed the highest release across the formulations except for M1, containing the least polymer concentration, which had a lower release rate than S1 but greater than P1 and the crude extract.

Release of extract from all the formulations including PREx in the first 5 min was between 0.06 and 95% with the crude extract having the least release and M3 exhibiting the highest release. However, release of extract at the end of dissolution test time (60 min) from all the solid dispersion formulations and physical mixtures was observed to increase appreciably; each formulation showed an increase in extract release with time, the values ranged between 17.07 and 100%. Conversely, PREx was found to have released < 1% at the end of the dissolution time.

Visual inspection of the formulations during dissolution revealed M3 to be completely dissolved producing a clear solu-



**Figure 2.** Differential Scanning Calorimetry thermogram of PREx (A), physical mixture of PREx and PEG 4000 (B), solid dispersion of PREx and PEG 4000 prepared by melt-fusion (C).



**Figure 3.** *In vitro* release profile of the different solid dispersion formulations, physical mixture, and extract alone.

tion while M1 and the crude extract showed very slow dissolution and produced residues due to incomplete solvation in the media. Formulation M1 (ratio 1:1) prepared by the melt-fusion method was observed to be sticky and formed agglomerates

after preparation and did not completely disintegrate in the dissolution media.

At the end of the dissolution time, M3 was observed to have complete release (100%) while P3 had about 83% and S3 had about 61% release.

**Modelling of extract release profile**

The release kinetics used to extrapolate the mode of extract release from all the formulations were Zero order, First order, Higuchi, and Hixson-Crowell models. The *in vitro* release model with the highest coefficient regression factor was deemed the best model; Table 4 shows that the kinetic release was best expressed by the Higuchi model with the highest regression factors. The Korsmeyer-Peppas release coefficient (n) was used to determine the mechanism of release from the formulations. Table 4 shows that solid dispersion formulations containing higher polymer concentration (S3 and M3) and the physical mixture with corresponding high polymer concentration (P3)

**Table 4. Kinetics and mechanism of PREx release from solid dispersion formulations.**

Formulations	Zero order	First order	Higuchi	Hixson-Crowell	Korsmeyer-Peppas	
	r <sup>2</sup>	r <sup>2</sup>	r <sup>2</sup>	r <sup>2</sup>	r <sup>2</sup>	n
S1	0.4958	0.2699	0.7123	0.2618	0.7275	0.9870
S2	0.3889	0.2784	0.6187	0.2741	0.6911	0.9035
S3	0.3903	0.2546	0.6100	0.2435	0.6851	0.7097
M1	0.2812	0.2880	0.4708	0.2875	0.6408	1.1134
M2	0.3703	0.2866	0.5620	0.2856	0.6806	0.8990
M3	0.3284	0.2948	0.5822	0.2397	0.6821	0.6856
P1	0.9209	0.2354	0.9220	0.2130	0.8586	0.9296
P2	0.1678	0.2956	0.3572	0.2985	0.6134	0.9489
P3	0.6287	0.0887	0.8622	0.0735	0.7648	0.7821
PREx	0.6174	0.2890	0.8542	0.2889	0.4900	0.1837

had “n” values between 0.6856 and 0.7821 while all the other formulations (S1, S2, M1, M2, P1, P2, PREx) had ‘n’ values between 0.8990 and 1.1134.

## DISCUSSION

The product yield from all the formulations was substantial and shows the efficiency of the preparation process. However, low product yields observed from the solvent-evaporation method could be attributed to the dissolving action of the solvent.

The spectrum of PREx (Figure 1A) was characterized by principal absorption peaks and broad characteristic peaks at 3596.9cm<sup>-1</sup> which corresponds to the stretching vibration band of O-H. This band is associated with polyphenolic compounds like tannins, flavonoids, and glycosides (Nagalakshmi & Anuradha, 2017; Olorunsola, Adedokun, Olisakwe, & Alozie, 2022). Peaks at 2113.4, 1599.0, and 1312.0cm<sup>-1</sup> reveal the presence of other functional groups; alkanes, ketones, and aromatic groups. A characteristic identity of the extract which is its peculiar fingerprint is revealed between 1021.3 and 708.2cm<sup>-1</sup>. The characteristic peak of the extract disappeared at 3213.9.0cm<sup>-1</sup> in Figures 1B and 1C (spectra of P3 and M3) but peaks at 2877.5 and 2881.2cm<sup>-1</sup> were observed which is attributable to the polymer (PEG). An earlier report has shown that PEG has a characteristic peak between 2800 and 2900cm<sup>-1</sup> which is associated with C-H stretching (Khairuddin et al., 2016) and this characteristic peak was observed in our results. Smoothing of the extracted peak in the presence of the polymer observed in Figures 1B and 1C suggests possible strong integration of the extract and the polymer in both the physical mixture (P3) and solid dispersion prepared by the melt-fusion method (M3). Although slight shifting, broadening, and reduction in peak intensity were observed in the solid dispersion mixtures (Figures 1B and 1C), no additional peaks were observed indicating that there was no chemical interaction between the extract and excipients used in the preparation of the solid dispersion formulations.

Differential scanning calorimetry (DSC) thermogram showed the thermal characteristics of the investigated samples. DSC

is capable of providing data about the molecular transition of molecules, conversions of different crystalline phases, and thermal stability of materials (Fernandes et al., 2013). The DSC thermogram shown in Figure 2 shows the differences in thermal characteristics which in turn demonstrates the impact of solid dispersion formulation on the physical characteristic of the extract. The lower onset melting temperature of M3 which was remarkably lower than that of PREx or P3 indicates rapid mobility of amorphous chains. Similarly, the low peak temperature and conclusion temperature of M3 compared to PREx point to the fact that the crystalline nature of the extract has been greatly diminished. Broadening of the extract’s endothermic melting peak in P3 could be attributed to the melting of small quantities of the extract signifying that a large percentage of the extract was incorporated in the polymer carrier (Bikaris et al., 2005). Conversely, the absence of the extract peak in M3 could suggest the dissolution of crystalline extract into the molten carrier resulting in transformation into an amorphous form or a lack of crystallinity of the extract in M3 (Xie et al., 2009). This confirms the dispersion of the extract at the molecular level in the polymer carrier matrix (Ghanem, Ali, El-Shanawany, & Ibrahim, 2013).

Our result is in tandem with the literature where the absence of the melting peak of an active drug correlated with the amorphous nature of the drug (Xie et al., 2009; Weerapol et al., 2017; Yen, Liang, Cheng, Hsu, & Wu, 2020). It also corroborates an earlier report that the decrease in intensity and shifting of sharp melting peaks of drugs in solid dispersion is an indication that the amount of crystallinity is considerably reduced, and the drug is present in an amorphous form (Sharma, Jain, & Tanwari, 2013).

The reduction in enthalpy of crystallization observed in the thermogram infers that the energy required to solubilize the extract in P3 is lower than that required to solubilize the crude extract (PREx) itself and much lower for M3.  $\Delta H$  is directly related to the crystalline nature of a material; it reflects the melting of the crystalline region in a material. A low crystalline melting temperature range ( $\Delta H$ ) indicates a reduction in crystalline linkages (Bhupender, Rajneesh, & Baljeet, 2013; Olayemi et al.,

2021; Unnisa et al., 2022). This shows that the extract in solid dispersion formulation had lost its crystallinity which is a precursor to the desired effect of improving the extract's aqueous solubility.

*In vitro*, the release profile of the formulations shows the extent of improvement in the rate of dissolution of the extract. As observed, agglomerates in formulation M1 did not readily get dispersed upon contact with water as such, M1 did not readily go into the solution. Thus, the entrapped extract in the polymer-drug matrix in M1 had a very low dissolution rate (Kale, Hapgood, & Stewart, 2009). On the other hand, the highest dissolution profile seen with M3 could be attributed to its amorphous nature as observed in the DSC thermogram which may be responsible for its rapid release. This is because lower kinetic energy was required to break any crystal lattices within the dispersion mixture leading to rapid release and improved bioavailability (Ghaste, Chougule, & Shah, 2009). Generally, the poor dissolution profile of the crude extract (PREx) was observed to be improved in the physical mixture and much more improved in the solid dispersion formulations. Improved dissolution of the extract is attributable to the hydrophilic properties of the carrier; PEG 4000 which includes increasing wettability, dispersibility of the poorly soluble extract, and surface area available for dissolution by reducing the interfacial tension between the extract and medium (Jigar, Jayvadan, & Jain, 2012). These features are thought to have led to possible molecular dispersion of the extract in the dissolution mixture leading to a marked dissolution rate of all the solid dispersion formulations. Furthermore, the incorporation of higher polymer concentrations produced a remarkable increase in extract release across the formulations.

The method of preparation of the solid dispersions was seen to greatly influence the rate of release from these solid dispersions. Solvent-evaporation method of solid dispersion is known to solubilize the drug and carrier at the molecular level while the fusion technique is said to improve molecular mobility between the drug and the carrier molecules, especially at the melting points of the components of the dispersion mixture (Pawar, Mundhe, Deshmukh, Pandhare, & Nandgude, 2021). Both methods are known to be good strategies for improving drug release but our result shows that the melt-fusion method was better at improving the solubilization of the crude extract of *Prosopis africana* stem bark. This is an advantage in further processing and probable commercialization because the melt-fusion method is a simple and economical process devoid of possible residual solvent in the formulation and high cost of preparation as a result of the solvent-evaporation method (Tran et al., 2019).

The coefficient of correlation ( $r^2$ ) from the plots was used to indicate the degree of curve fitting and values approaching 1 were used to determine the predominant dissolution profile fitting to the mathematical equation. Interpretation of the *in vitro* release data as determined by the Higuchi model which produced the highest  $r^2$  values suggests that the kinetic release was accomplished by diffusion from the porous matrix system of the polymer and extract in the solid dispersions upon con-

tact with the dissolution fluid (Hamid, Harris, Jaweria, & Rabia, 2006; Azadi, Hamaid, & Rouini, 2013). On the other hand, the Korsmeyer-Peppas model was applied to determine the mechanism of release from the formulations and the release diffusion coefficient ( $n$ ) was used to characterize the mechanism of release. When the " $n$ " value is 0.45, it indicates the release is diffusion-controlled which is also known as Fickian diffusion. Values  $\geq 0.89$  indicate swelling-controlled release (Case II or Super-case II transport) while " $n$ " values between 0.45 and 0.89 indicate Non-Fickian or anomalous diffusion which is a superimposition of the other two mechanisms (Siepmann & Peppas, 2001). The extract release for M3, P3, and S3 was found to be Non-fickian/anomalous diffusion which was characterized by the movement of the dissolution fluid into the dispersion matrix at constant velocity leading to an increase in the amount of fluid absorbed with time. This corresponds to the fact that extract release was controlled by simultaneous diffusion out of and erosion of the dispersion matrix (Azadi et al., 2013; Gouda, Baishya, & Qing, 2017). The fast dissolution of these formulations could be ascribed to the possible conversion of the crystalline extract into its amorphous form thus making dissolution faster as shown by the DSC thermograms. Extract release from the other formulations (S1, S2, M1, M2, P1, P2, PREx) was indicative of super case II transport signifying that drug release was primarily by swelling of the polymer matrix, which is accompanied by slow drug release. This could be the reason why drug release from these formulations was slower than those of S3, M3, and P3 as observed in the *in vitro* dissolution test. This suggests that release of the extract was complicated by molecular relaxation and functional interaction between the fluid and the dispersion matrix (Odeku, Okunlola, & Lamprecht, 2013; Camelo, Franceschi-Messant, Perez, Girod, & Ré, 2016). The result shows that release from the optimized formulation (M3) was by super-imposition of swelling and then diffusion mechanism.

## CONCLUSION

In this study, solid dispersion formulations of the methanol stem bark extract of *Prosopis africana* (PREx) were successfully prepared by solvent evaporation and melt-fusion using the hydrophilic polymer; polyethylene glycol 4000.

DSC analysis results showed the transformation of extract crystallinity into its amorphous form, dissolution studies also indicated improved solubility of PREx. Significant enhancement of dissolution of the extract was obtained from formulations prepared by the melt-fusion method containing the highest polymer concentration; 98% release was achieved at the end of 30 min. This shows the possibility of enhancing dissolution of the poorly water-soluble *Prosopis africana* extract by solid dispersion however, substantiating this effect by clinical evaluation could broaden its application as a potential therapeutic agent.

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