About the Journal

Focus and Scope

Pharmacy Education journal provides a research, development and evaluation forum for communication between academic teachers, researchers and practitioners in professional and pharmacy education, with an emphasis on new and established teaching and learning methods, new curriculum and syllabus directions, educational outcomes, guidance on structuring courses and assessing achievement, and workforce development. It is a peer-reviewed online open access platform for the dissemination of new ideas in professional pharmacy education and workforce development. *Pharmacy Education* supports Open Access (OA): free, unrestricted online access to research outputs. Readers are able to access the Journal and individual published articles for **free** - there are no subscription fees or 'pay per view' charges. Authors wishing to publish their work in *Pharmacy Education* do so without incurring any financial costs.

In addition we are listed in EBSCO, and indexed in the Emerging Sources Citation Index (ESCI - Web of Science), EMBASE and SCOPUS.

The Journal also recognises the importance of policy issues and current trends in the context of education, professional development and workforce.

The Journal publishes reports of research and innovation in all aspects of professional pharmacy education and training, case studies, country studies, innovations in laboratory and professional educational practice, workforce issues and development, reviews and reports on information technology in education and reviews of current literature.

The Journal has a clear international perspective, and has a longstanding policy of facilitating publication, in particular for younger Faculty, and those authors whose first language may not be English, and manuscripts from all regions seeking low cost engagement with the wider global community.

The Journal is published by the International Pharmaceutical Federation (FIP) and is aligned to the global mission of advancing education, advancing practice and advancing science.

Peer Review Process

Pharmacy Education has adopted a double-blind peer review process - the identities of the Authors and Reviewers are kept from being known to each other. A step-by-step checklist is provided for Authors, Reviewers and Editors to ensure this (see Ensuring a Blind Review).

Peer Review Process: Once a submission is received, the assigned Editor will select appropriate Reviewers based on their expertise and proven ability to critique. The peer reviews received will assist the Editor in determining the validity, significance and originality of the work submitted. Reviewers will also provide comment on manuscript content for scientific value, check for adherence to general scientific practice as well as *Pharmacy Education's* specific guidelines. The Peer Review process will look closely at methodology and the data validity, and consider the ethical approach. Reviewers are encouraged to provide suggestions for improvement and recommend to Editors if manuscripts should be accepted, accepted with revisions, or rejected.

Please note that an invitation for Authors to submit a revised version is not a guarantee of acceptance. Ultimately, the final decision lies with the Editor assigned to each submission. An Editor can reject any article at any time before publication, including after acceptance if concerns arise about the integrity of the work.

As part of their agreement with *Pharmacy Education,* Reviewers will keep manuscripts and associated material strictly confidential, and will not appropriate Authors' ideas before the manuscript is published. Once a review has been completed, Reviewers will be directed and expected to permanently delete/destroy any retained copies of manuscripts they hold (see Privacy Statement).

Timeliness: Reviewers are expected to respond promptly to requests to review and to submit reviews within the time agreed. Reviewers are also required to declare their conflicts of interest and recuse themselves from the Peer Review process if a conflict exists. Editors will do their utmost to ensure timely processing of manuscripts. Authors will be notified on any unusual delays in publication of manuscripts via email. Authors will ne notified as soon as possible if a manuscript is going to be rejected, either by the Journal Manager or Editorial Team.

Journal Ownership and Editorial Scope

Pharmacy Education is published by the International Pharmaceutical Federation (FIP). Appointments and dismissals to the Editorial Team are made by the Editor-in-Chief in consultation with FIP.

Editorial roles and responsibilities

Editor-in-chief - The Editor-in-Chief has full authority over content publication in *Pharmacy Education.* In co-operation with the wider Editorial Team and publisher, they direct overall strategy of the journal. Together with the Editors and Associate Editors, the Editor-in-Chief reviews and decides upon submitted manuscripts, ensuring timely publication of submissions.

Editors and Associate Editors – Editors and Associate Editors are appointed for a three (3) year term to the Editorial Team. Their responsibilities include, but are not limited to, decision making based on peer review feedback, recommending appointments to the Reviewer Board, and responding to editorial enquiries.

Advisory Board – *Pharmacy Education* is currently engaged in establishing an Advisory Board who alongside the Editor-in-Chief, Editors and Associate Editors will assist with:

- Guidance on the peer review and publishing policies of Pharmacy Education and where necessary, suggest reviewers to the Editor-in-Chief.

- Developing the journal by providing expertise to the Editor-in-Chief and FIP on how to increase impact and reach

- Impartial Judgement in appeal cases by providing professional, independent scientific comments to the Editor-in-Chief and FIP

- Promoting *Pharmacy Education*

Managing Editor – The Managing Editor assumes day-to-day responsibility of managing the submissions flow to *Pharmacy Education*. They liaise with Authors and Reviewers where needed, clarifying the Submission and Publication process as well as responding to all general enquires. The Managing Editor also completes all typesetting, proofreading and online publication of accepted manuscripts once accepted by the Editors.

Advertising in Pharmacy Education

Pharmacy Education does not provide opportunities for advertising on any of its platforms, including downloadable content. This policy maybe reviewed in future in conjunction with the publisher, FIP.

Competing Interest Guidelines

To assist *Pharmacy Education* in ensuring public trust in the scientific process and the credibility

of articles that it publishes, all those involved in the Submissions and Peer Review process are required to disclose perceived as well as actual conflicts of interest.

Authors: When submitting an article to *Pharmacy Education*, all Authors are required to disclose all financial and personal relationships that may bias their work (see Submission Preparation Checklist)

Peer Reviewers: Reviewers are asked at the time of conducting a review if they have conflicts of interest that may impact on their ability to provide an unbiased review. Reviewers are asked to disclose conflicts of interest to the assigned Editor. The assigned Editor will then cancel the review and reassign the article to another reviewer. Reviewers agree to not use knowledge of the work they are reviewing before its publication to further their own interests.

Editors and Journal Staff: Editors making final decisions on manuscripts will recuse themselves where conflicts of interest or relationships that pose potential conflicts are present. All editorial staff (including guest editors) provide the Editor-in-Chief with a completed Editorial Disclosure Form (up to date description of financial interests/conflicts). Editors will annually publish disclosure statements about potential conflicts of interests related to the commitments of journal staff.

Research involving Human participants and Informed Consent

It is the responsibility of the authors to ensure that research involving human subjects has been reviewed and approved by the appropriate research or ethics review committee, or that it has been determined to be exempt from such review.

Confirmation of this should be included in the Cover Letter and also included in the Methods section of the manuscript. Where informed consent is required, authors should include a statement in the manuscript detailing that informed consent was obtained from human subjects (see Submission Preparation Checklist)

Article Corrections, Replacement, Retractions & Removal Policy

Published articles are a permanent record that should remain unaltered. However, *Pharmacy Education* recognises that in exceptional circumstances, articles may need to be corrected, replaced, retracted or removed.

The Editor-in-Chief has full authority over content publication in *Pharmacy Education*. In making decisions regarding publication, the Editor-in-Chief is guided by the policies of the Journal as well as legal requirements such as libel, copyright, infringement and plagiarism.

Corrections

Detailed below are our procedures for managing requests for corrections post publication

Minor errors

If Authors identify a minor error once an article has been published online, they are advised to email their request for corrections to *Pharmacy Education* for consideration.

Minor errors include: errors in spelling, data, medical terms; missing text; amendments to tables, figures or appendices; errors in correspondence details, etc. The Journal may decline proposed corrections that are for aesthetic reasons; errors to text, typography tables, figures and appendices if the meaning is unchanged; errors in acknowledgments lists *etc*.

Significant Corrections

Corrections may be needed if honest errors have resulted in a portion of an article being misleading; if the author/contributor lists are disputed; or if potential conflicts of interest affecting authorship are disclosed post publication.

Where the Editor-in-Chief agrees that a correction is needed, the Journal will:

- Correct the error online, and to any article file for download, linking to a **Correction Notice** via a footnote

- The **Correction Notice** will detail the changes made to the original version, and the dates the changes were made.

Replacement

Honest errors such as mis-classification or miscalculation may lead to significant changes to the results, interpretations and conclusions. In such cases, the Journal will consider retraction with replacement of the article:

- The changed version of the article will undergo further editorial review;

- The authors will be required to detail and explain the changes made which will be published as supplementary material or in an appendix;

- The supplementary material/appendix will be attached to the changed version, allowing for

complete transparency.

Retraction

An article will be retracted if the results or conclusions are unsound and/or where misconduct breaching professional ethical codes has occurred. The publisher and Editor-in-Chief will conduct an investigation into the errors or misconduct before retracting an article. The following steps will be taken where articles are retracted:

- A **Statement of Retraction**, giving the reasons for the retraction and signed by the authors and/or the Editor-in-Chief will be published online linking to the original article.

- The original article is preceded by a screen containing the **Statement of Retraction**. The reader can then proceed to the article itself.

- A watermark will be added to the original PDF indicating on each page that it is “RETRACTED”

- The **Statement of Retraction** will be included as a numbered page in the Table of Contents to ensure proper indexing, and will include the article title in its heading

Removal

Very occasionally, it may be necessary to remove an article from the online database as a consequence of legal action (*e.g.*, defamatory content, infringement on legal rights, article is subject of a court order, or might pose a serious health risk if an article's content is acted upon).

In these circumstances:

- The article's metadata (title and author details) will be retained and the text replaced with an **Article Removal Notice**

- The **Article Removal Notice** will be included in the Table of Contents and prefix the metadata.

Expressions of Concern

If concerns or allegations of misconduct regarding a publication are raised, the Editor-In-Chief will consult the Committee on Publication Ethics (COPE) http://www.publicationethics.org and

initiate the appropriate procedure based on the nature of the concern or allegation. The Editor-in-Chief, with appropriate support form the Editorial Team, will assess each situation individually.

The Editor-in-Chief will consider issuing an **Expression of Concern** if:

- the Editor judges that readers should be made aware of potentially misleading information contained in a published article;

- investigations into any concerns of misconduct remain inconclusive;

- concerns remain over the impartiality of any investigations into alleged misconduct;

-an investigation is pending and a judgment is not expected for some time.

An **Expression of Concern** will be published and appear in the Table of Contents and include the title of the article in its heading. It should be noted that *Pharmacy Education* understands the potential repercussions that issuing an **Expression of Concern** can bring and will only take this action where it is deemed necessary.

If an investigation produces evidence of misconduct or reveals that the concerns raised are well founded after an **Expression of Concern** has been published, the Journal will instigate the Retraction process

Appeals and Complaints

Appeals

Authors are entitled to appeal editorial decisions if they believe their submission has been unfairly or inappropriately rejected. An appeal letter should be submitted to the Journal Manager (pej@fip.com)

The appeal letter should provide appropriate detail and context. For example, if an Editor has provided peer review comments it is worthwhile responding to each item in the letter. If the appeal is against the editorial decision made on the submission, explaining and justifying clearly the work's importance, relevance, and usefulness in the appeal letter is recommended.

An invitation to submit a revised version after sending an appeal letter does not guarantee acceptance; the revised article will proceed through the Peer Review process again.

Appeal letters will be ordinarily acknowledged within 5 working days, followed by a full response

containing the appeal decision within 4 weeks.

Complaints

Pharmacy Education aims to respond quickly, courteously, and constructively to complaints about the Journal's procedures, policies, or actions.

Complaints will be considered if:

- the complainant defines their dissatisfaction as a complaint; *and*

- it concerns a failure of process, *i.e.* a long delay or a severe misjudgement; and is not simply disagreement with an editorial decision;

- the issue being raised is within the responsibility of *Pharmacy Education*'s editorial remit

Complaints should be directly emailed to the Journal Manager (pej@fip.com) who will ordinarily formally acknowledge receipt within 5 working days.

- The Journal Manager will forward the complaint to a relevant person within the Journal organisation who will aim to provide a full response within four weeks. If this is not possible, an interim response and update will be given within the four weeks.

- Following this action, if the complainant remains unhappy, complaints will be escalated to the Editor-in-Chief whose decision is final.

- If a complainant remains unhappy, they may complain to an external body such as the **Committee on Publication Ethics** (COPE) http://www.publicationethics.org. They will consider complaints against Editors once a Journal's own Complaints procedures have been exhausted.

Whistleblowing

Pharmacy Education recognises that there may be legitimate reasons for individuals who wish to remain anonymous when raising issues relating to publication ethics. Concerns or allegations raised anonymously will be handled as they would be if the complaint were from another source, following the processes and procedures of the Journal.

If concerns remain after processes have been followed, The Editor-in-Chief will seek advice from **Committee on Publication Ethics** (COPE) http://www.publicationethics.org

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Journal History

Pharmacy Education has been publishing peer reviewed education, training, research and evaluation in the field of pharmaceutical education since 2000.

The Journal encourages manuscript submissions from younger career scientists, academics and practitioners and has a focus on supporting authors who do not have English as a first language.

Through our FIP publication platform we are able to reach out to over 3 million pharmacists and pharmaceutical scientist worldwide.

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IAI SPECIAL EDITION

RESEARCH ARTICLE

Influence of dispersing solvent on curcumin dissolution from solid dispersions prepared using hydroxypropyl methylcellulose-polyvinylpyrrolidone K30

Dewi Setyaningsih, Dyah Roro Palupi, Yustina Sri Hartini
Faculty of Pharmacy, Sanata Dharma University, Yogyakarta, Indonesia

Keywords
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Correspondence
Dewi Setyaningsih
Faculty of Pharmacy
Sanata Dharma University
Yogyakarta
Indonesia
dewi@usd.ac.id

Abstract

Background: Preparation of lipophilic compounds into solid dispersion formulations (SDs) has been credited with increasing their dissolution rate. Understanding the role of the dispersing solvent is crucial to the SDs preparation. Drug/carrier-solvent immiscibility may decrease the dissolution rate. **Aim**: This work aimed to study the effect of different dispersing solvents on a curcumin dissolution. **Method**: A solvent evaporation method was used in the SD preparation. The formulation was prepared at 30% w/w drug load contained *Curcuma longa* and a carrier mixture of Hydroxy Propyl Methylcellulose (HPMC)/ Polyvinylpyrrolidone K30 (PVP K30). As for the dispersing solvent, the study used ethanol, ethyl acetate, and ethanol/ethyl acetate solvent mixture. The dissolution profile was obtained and analysed for the dissolution-efficiency (DE). **Result**: The DE values of 38.5%, 37.8%, and 32.0% were obtained using ethanol, ethyl acetate, and ethanol-ethyl acetate mixture. **Conclusion**: The results show that there is a significant impact of using different SD solvents on curcumin dissolution.

Introduction

Curcuminoids are natural polyphenolic compounds. Curcuminoid is the collective name for three components of *Curcuma longa,* i.e. curcumin, dimethoxy curcumin, and bis-dimethoxy curcumin. Within this group of curcuminoids, curcumin is the major compound (Nelson *et al.*, 2017). Numerous shreds of evidence have been reviewed on the therapeutic potential of curcumin, especially the ones related to its anti-oxidant and anti-inflammatory properties (Tabrizi *et al*., 2019). However, its poor bioavailability after oral administration limits the function of curcumin in a clinical setting (Gupta, Patchva, & Aggarwal, 2012).

Many reasons have been proposed to account for the poor oral bioavailability of curcumin, e.g., instability issue and rapid metabolism. However, poor water solubility and dissolution are the most reported description of its poor bioavailability for curcumin. The strong inter-and intra-molecular hydrogen bonding between curcumin molecules contributes to its remarkably low solubility and dissolution rate in water (Qi, Chang, & Zhang, 2008).

The study applied the technical method of solid dispersions (SDs) to improve the solubility of curcumin. Thus, it also increases the absorption of the drug in the gastrointestinal tract. SDs are defined as the dispersion of one or more active ingredients in a hydrophilic matrix, and it is prepared by fusion or solvent evaporation method employing lyophilisation, spray drying, or vacuum rotary evaporator (Leuner & Dressman, 2000). The mechanism underpinning solubility enhancement in SDs might be due to particle size reduction, improved wetting, an opportunity of dispersion at a molecular level, or through amorph formation (Janssens & Van den Mooter, 2010).

SDs produced via the solvent evaporation method involve dissolving lipophilic drugs and the carriers in a solvent or solvent mixture, followed by an evaporation method. Drug release during a dissolution study can be

rationally correlated with the variant of dispersing solvents or solvent mixtures used before the evaporation step (Rizi *et al.*, 2011). It was reported by Chen and colleagues (2018) that the dissolution rate of felodipine was affected by the solvent type; the highest dissolution rate was achieved by dispersing the drug in ethanol-dichloromethane compared to the organic solvent alone (Chen *et al*., 2018). Understanding drug-carriers-solvent miscibility is necessary because liquid-liquid phase separation can occur in the drying step, which might lead to crystal formation resulting in poor water solubility and dissolution. Therefore, this study aimed to investigate the impact of different organic solvents (ethanol, ethyl acetate and ethanol-ethyl acetate solvent mixture) on curcumin dissolution in SD formulations of *C. longa* extract-PVP K30/HPMC.

Materials and methods

Curcumin as a reference standard (USP) with a purity of 98% was obtained from Sigma-Aldrich (St. Louis, United States). *C. longa* extract was given by PT Phytochemindo Reksa Bogor, Indonesia. PVP K30 was provided by PT Konimex, Solo, Indonesia. HPMC and PVP K30 were supplied by PT Konimex (Solo, Indonesia). Pro-analytical grades of methanol, ethanol, ethyl acetate, Sodium lauryl sulfate (SLS), and sodium dihydrogen phosphate were obtained from Merck (Darmstadt, Germany). Water was prepared using a Milli-Q IQ water purification system.

Preparation of the solid dispersions formulation (SDs)

Ethanol, ethyl acetate, and ethanol/ethyl acetate mixture of 1/1 (v/v) were used as the dispersing solvents to prepare the drug-carrier mixtures. The carrier was a PVP K30/HPMC mixture in a 2:1 weight ratio. Table I shows the composition of solid dispersions preparation. The final concentration of the dissolved material (*C. longa* + PVPK30/HPMC) was 11.1 mg/mL, while the drug load was designed for 30% (w/w) of curcumin as calculated in the dried product.

Table I: The composition used in the solid dispersion preparation

Formula	System	*C. longa* extract (g)	PVP K30 (g)	HPMC (g)	Organic solvent (ml)	Water (ml)
1	E	1.500	2.334	1.166	375	75
2	E-Ac	1.500	2.334	1.166	375	75
3	E/E-Ac (1/1)	1.500	2.334	1.166	187.5:187.5	75

E = ethanol; **E-Ac** = ethyl acetate.

The Buchi Rotavapor R-300 evaporated the solvent (Buchi, Flawil, Switzerland) at 50°C and vacuum pump setting of 175 mbar for ethanol or ethanol-ethyl acetate mixture and 240 mbar for ethyl acetate. The obtained samples were subsequently dried in a vacuum oven at 50°C for another 24 hours. The dried product was grounded in a mortar and sieved using 60 mesh (Kaewnopparat *et al*., 2009). After that process, the yield was determined. The dried SD sample was stored in a desiccator until use. The drug load of the SD formulations was determined by dissolving the dried SD samples in methanol followed by detection in a UV-Vis spectrophotometry (Shimadzu 1800, Shimadzu Co. Ltd., Kyoto, Japan) at 420.5nm. The curcumin content was quantified based on a calibration sample in which it demonstrates the linear equation of y = 0.1278x + 0.0246 at the correlation coefficient of 0.9990.

Preparation of Physical Mixture (PM) sample

The control experiment used the PM sample. To prepare the PM sample, *C. longa* extract and PVPK30/HPMC at a 2:1 weight ratio were simply mixed using mortar and pestle. The powder was sieved through 60 mesh size before use (Kaewnopparat *et al*., 2009).

Dissolution study

In this study, the SD and PM formulations were tested on a SOTAX AT7 USP type II dissolution tester. The dissolution test was performed in 900 mL of 0.5% SLS in 20mM sodium phosphate buffer at 37 ± 0.5°C with 75rpm agitation. In order to maintain a sink condition, 5.0mL of dissolution medium was sampled at regular intervals. It was detected using a UV-Vis spectro-photometer at 430nm (Shimadzu 1800, Shimadzu Co. Ltd., Kyoto, Japan). Plotting the absorbance against the calibration equation of y = 0.1556x + 0.0043 yielded the curcumin concentration. The dissolution profile obtained in the 150 minutes study was analysed using a dissolution efficiency (DE) approach based on the equation below.

$$DE_t = \frac{\int_{t1}^{t2} y.\,dt}{y_{100}.\,t}) \times 100\%$$

DE_t: Dissolution efficiency at a time (t); y: Area under the curve of the dissolved drug at time t; y_{100}.t: Rectangle area where 100% of drug dissolved at time t

Results

Different solvents resulted in yield variation. The yield of SD products were 62.8%, 75.6%, and 66.0% for ethanol, ethyl acetate, and ethanol/ethyl acetate (1:1).

The colour of dried powder varied according to different solvents (Figure 1). Ethanol results in brownish-yellow colour (Figure 1a), ethyl acetate and ethanol-ethyl acetate mixture result in yellow colour (Figure 1b,c).

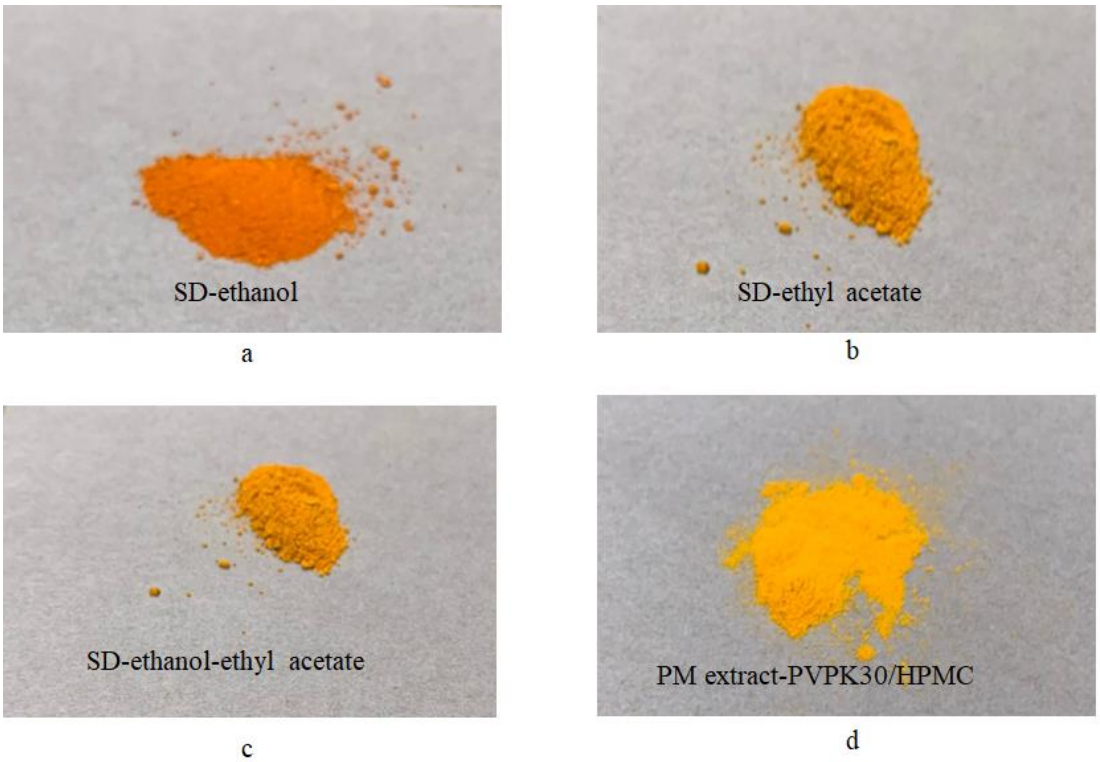

Figure 1: The SDs powder resulted from different solvents, i.e a) ethanol, b) ethyl acetate, c) ethanol/ethyl acetate (1:1). Physical mixture (PM) serves as a control experiment (d)

Drug load

Table II presents the drug load data as recovery values. The percentage assay values, calculated based on the recovery test at which the obtained curcumin contents were divided by the theoretical values and multiplied by 100%. The PM, which was used as control formulation, demonstrated a drug load of 91.34 ± 0.24% w/w of curcumin. Varied recovery values were observed depending on the organic solvent used in the solubilisation process in the SD preparation.

Table II: Drug load of the formulation presented as recovery value

Formulation/solvent	Recovery (%)	SD (%)
PM	91.34	0.24
E-OH	85.88	0.45
E-Ac	92.15	2.09
E-OH/E-Ac (1:1)	110.66	0.33

PM = Physical Mixture ; E-OH = ethanol; E-Ac = ethyl acetate; Data were obtained from three replications.

Dissolution

Figure 2a shows the dissolution profile of curcumin from the SD formulation prepared by ethanol, ethyl acetate, ethanol/ethyl acetate mixture of 1:1 volume ratio, and the PM formulation. Up to 150 minutes of monitoring, the SDs formulation in the binary carrier of PVP K30/HPMC at a weight ratio of 2:1 was able to increase curcumin dissolution as compared to the PM formulation. Using different organic solvents to disperse *C. longa* extract in the SD processing step resulted in variation in the amount of curcumin released in the dissolution media. DE_{150} was used to judge the release profile (Figure 2b). SD prepared using ethanol, ethyl acetate, and ethanol/ethyl acetate mixture of 1:1 volume ratio demonstrates DE_{150} of 38.46±0.08%, 37.83±3.68%, and 31.98±1.13%. The DE_{150} values resulted from ethanol and ethyl acetate as the SD solvent does not differ significantly (p>0.05).

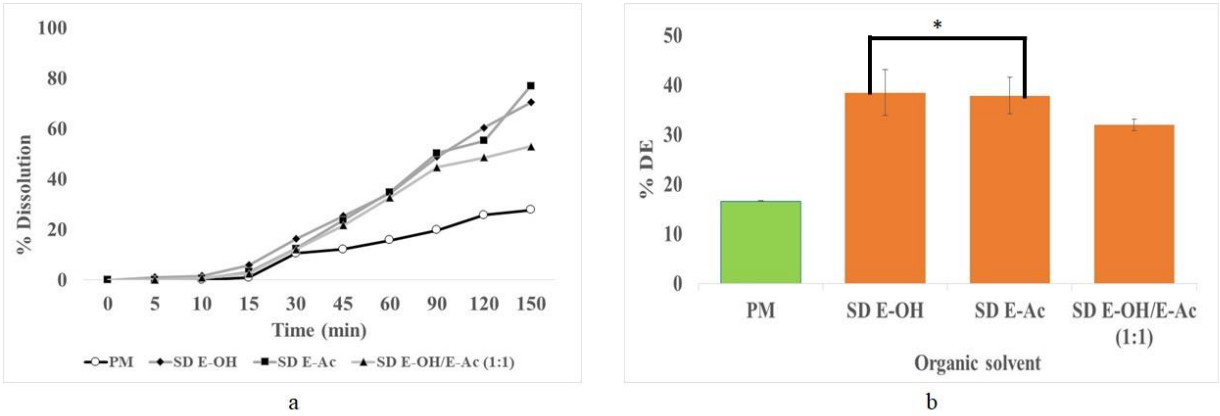

Figure 2: Dissolution profile (a) and DE150 (b) values. *No significant difference; Data is presented as mean and SD of n =3

Discussion

The solvents used in the preparation step, as reported in the SD preparations, were varied, such as ethanol, methanol, dichloromethane and acetone and it was found that the solvent type affected the physicochemical properties and dissolution of lipophilic drugs (Dohrn *et al*., 2021). Among them, ethanol was reported as the most popular solvent. Furthermore, in a more specific mechanism, it was suggested the drug release as observed in the dissolution study could be affected by the interaction of drug-solvent through the opportunity of being a proton donor and/or a proton acceptor to facilitate the miscibility of drug carries in a selected solvent. The previous research reported that the solvent type could affect the physicochemical properties of the SDs product as well as the dissolution behaviour (Krstić *et al*., 2020). The effect of the miscibility of drug-polymer in different organic solvents as dispersing solvent on the physical properties and stability of SD Naproxen-PVP K25 was studied; acetone was reported as the best dispersing solvent over methanol and acetone-methanol blend in the preparation of the SD (Paudel & Van den Mooter, 2012).

This study investigated the influence of solvents used to solubilise the lipophilic compound (curcumin) on the physical characteristic of SD curcumin-PVP K30/HPMC. Using different types of solvents, the SD preparation resulted in a various percentage yield. Ethanol resulted in the lowest yield compared to ethyl acetate or ethanol/ethyl acetate mixture. The use of ethyl acetate as the solvent in the preparation of SD formulation obtained the highest yield.

Figure 1 depicts the colour of the dried SDs product. The SDs powder produced in ethanol showed a more vivid tint of brownish-yellow colour. Turmeric's orange hue comes from curcumin and other curcuminoids. The pH of ethyl acetate is 6.5, while the pH of ethanol is 7.0. Curcumin can be decomposed to ferulic acid and feruloyl methane in neutral or alkaline circumstances, with feruloyl methane forming a brownish-yellow condensation result (Tonnesen & Karlsen, 1985). The SD produced in ethanol revealed a brownish-yellow colour (Figure 1), which could indicate a shift in the chemical structure of curcumin when the pH level changes, particularly when it becomes more alkaline. The lowest drug load (85.9% w/w) in SD produced in ethanolic solution could be attributed to modest curcumin degradation during the preparation.

To accurately compare the dissolution profile, the DE_{150} value obtained from the 150 minutes dissolution study was employed and is presented in Figure 2b. Preparation into the solid dispersions formulation using a PVP K30/HPMC as binary mixture carrier enhances the dissolution rate of curcumin compared to the physical mixture formulation (Figure 2a and Figure 2b). Ethanol is the common solvent employed in the SDs preparation using solvent evaporation method since ethanol is relatively safe as ethanol is in the Joint FAO/WHO Expert Committee on Food Additive (JEFCA) list as a suitable solvent for extraction (FAO, 2006). Furthermore, ethanol belongs to class III of the Food and Drug Administration (FDA) solvent list, considered as low toxicity potential to humans. Ethyl acetate is another member of class III solvent on the FDA list of solvent classification (Martin *et al.,* 2013).

In this study, using ethyl acetate as a solvent in the solubilisation process for the SD preparation of curcumin-PVP K30/HPMC results in a similar dissolution rate to that prepared with ethanol (Figure 2b). However, when these organic solvents were mixed at a 1:1 volume ratio of ethanol/ethyl acetate, the dissolution profile decreased as can be seen in the DE_{150} value of 32.0%.

The lower DE_{150} value of the SD-ethanol/ethyl acetate solvent mixture might be due to the less solubility of

curcumin-PVP K30/HPMC in the ethanol/ethyl acetate at 1:1 volume mixture (Krstić *et al.*, 2020).

Conclusion

The solid dispersions approach using a mixture of the binary carrier of PVP K30/HPMC in a solvent evaporation method increases the dissolution of curcumin compared to the physical mixture formulation. The use of various organic solvents to solubilise the lipophilic compound curcumin affects the dissolution behaviour of curcumin. Ethyl acetate results in higher yield, recovery value in drug loading evaluation, and dissolution profile of curcumin as indicated by the DE_{150} value.

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