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Application of FTIR-ATR Spectroscopy in Combination With Multivariate Analysis to Analyze Synthetic Drugs Adulterant in Ternary Mixtures of Herbal Medicine Products

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ABSTRACT

A rapid, efficient, inexpensive method is required to counter the increasing number of adulteration reports in herbal medicine products in Indonesia, specifically Jamu in a powder dosage form. This study aims to develop an approach for the quantification and classification of the adulterated herbal medicine product with synthetic drugs (prednisone and metamizole) using FTIR Spectroscopy and multivariate calibrations of partial least square regression (PLSR) and principle component regression (PCR) and discriminant analysis (DA). The spectra data of three individual pain reliever herbal products were scanned and collected by FTIR-ATR in mid-infrared region and further analyzed by two multivariate calibrations to exhibit the optimum mode for the quantification of each sample pain reliever herbal product. Based on statistical parameter value, PCR demonstrated the highest value of R^2 in both calibration and validation, and the lowest values of root mean square of calibration (RMSEC) and root mean square of prediction (RMSEP). DA could classify pure pain reliever herbal medicine products without any drugs and those adulterated with synthetic drugs. DA could discriminate between adulterated and unadulterated pain reliever herbal medicine products with 100% accuracy level. FTIR-ATR spectroscopy in the mid-infrared region coupled with chemometrics could be a potential analytical technique to detect synthetic drug contaminants in herbal products.

Keywords: Mid-infrared, multivariate calibrations, Jamu, synthetic drugs, pain reliever herbal

INTRODUCTION

Herbal medicine is widely known for being harmless, safer, has minor side effects, and cheaper than synthetic drugs. As one of the tropical countries, Indonesia has 5000 variations of researched medicinal herbs about the benefit for health written in Medicinal Herbs Index (Elfahmi *et al*., 2014; Ernst, 2002; Sim *et al*., 2004). Small-large industrial herbal industries in Indonesia formulated, produced, and sold the herbal medicine further consumed by the consumer. Indonesia's traditional herbal medicine, named Jamu, had various effects of maintaining the body health or curing the disease, like analgesic, anti inflammation, antirheumatic, antidiabetic, erectile dysfunction, and immunity supplement (Al Lawati *et al*., 2017; Vaysse *et al*., 2010). Based on collected data, herbal medicine products as pain relievers were the highest purchased and consumed product (Gitawati, 2013).

Herbal medicine as pain relievers in Indonesia was commonly named Jamu Pegel Linu (JPL), Jamu Encok (JE), Jamu Sakit Pinggang (JSP) contained herbs that empirically benefitted pain relievers such as back pain, joint pain, and muscle ache. The National Agency for Drug and Foods

report that finding the contaminant in herbal medicine raised primarily synthetic drugs contaminants. Uncontrolled dosage, amount, and usage of synthetic drugs lead to many unwanted adverse effects (Ariffin *et al*., 2021). An efficient, effective, rapid, and generous analysis technique is needed to counter the development of adulterated herbal medicine by drugs (Ching *et al*., 2018). Mid-infrared (MIR) region on FTIR spectroscopy, included as green analytical chemistry, performed a sophisticated method to analyze the synthetic drugs adulterant in herbal medicine products. The unique functional groups appearing in each wavenumber could provide information about molecular structure and composition. Coupled with multivariate analysis, FTIR spectroscopy could maximize the utility of distinguishing an adulterant in herbal products. The recent study reported using MIR amalgamated with principal component analysis (PCA) to identify anorectic and laxative adulterants in counterfeit slimming herbal medicines. Hence, the combination of FTIR spectroscopy and multivariate analysis seems promising (Cebi *et al*., 2017; Feng *et al*., 2014; Rooney *et al*., 2015).

The previous study demonstrated a good result for identifying metamizole adulterants in relieving herbal pain products in binary mixtures using MIR and multivariate analysis (Fatmarahmi *et al*., 2021). Research by Feng *et al*. (2014) used vibrational spectroscopy in the NIR region to detect anti-hyperglycemic drugs in herbal medicines for hypoglycemia. However, the literature reported on ternary mixtures in adulteration herbal products is limited. Therefore, this study demonstrated the performance of FTIR spectroscopy coupled with multivariate analysis (PCR, PLSR, and discriminant analysis) to detect adulterant drugs (Prednisone and Metamizole) in ternary mixtures with relieving herbal pain medicines.

MATERIAL AND METHODS

Materials and instrument

A registered pain reliever herbal product by the National Food and Drug Agency was purchased from the certified Traditional Herbal Industries in Indonesia. PT Phapros granted synthetic analgesic and antiinflammatory drugs. Aceton p.a. from Merck with catalog number 1.00014.2500. The instrument used FTIR-ATR Thermo Scientific Nicolet iS10 spectrophotometer for collecting infrared spectra data.

Sample preparation

Three pain reliever herbal products (JPL, JE, and JSP), in powder dosage forms, were purposefully adulterated by Prednisone and Metamizole in ternary mixtures. The known sample concentration series for calibration and validation (prediction) as quantitative analysis parameters were prepared. Eleven samples of each type of pain reliever herbal product in ternary mixtures with drugs were accurately scannned at concentrations 0-100% (wt/wt). The spectra were further analyzed by Partial Least Square Regression (PLSR) and Principal Component Regression (PCR). The selected condition was determined by statistical parameters performance, including R^2, Root Mean Square Error of Prediction (RMSEP), and Root Mean Square Error of Calibration (RMSEC). The prepared samples were also used for Discriminant Analysis as a pure and counterfeit category.

Infrared spectroscopy measurements

FTIR-ATR Thermo Scientific Nicolet iS10 spectrophotometer using DTGS (Deuterated Triglycine Sulfate) as element detector aided with Omnic software for a controller was used for collecting spectra of samples. All samples were scanned and recorded in the mid-infrared region (4000-650cm^{-1}) with a resolution of 8 cm^{-1}, accumulating 32 scans/min. The spectrum acquisition was repeated three times in the same and controlled condition. The background air spectrum was collected first before sample measurement to reduce the effect of different reference spectrums of the air. The crystal ATR was cleaned by acetone pro analysis (p.a.). According to Lambert-Beer law, the samples were directly compressed on ATR crystal and recorded in absorbance mode.

Chemometric analysis

Multivariate Calibrations and discriminant analysis were processed using TQ Analyst software version 9. Discriminant analysis was performed for qualification analysis. In addition, multivariate calibrations used for quantification were PCR and PLSR. The obtained spectrum data were divided into calibration sets and validation sets. Several ranges of wavenumber regions and the derivatization were performed to show the best prediction model for multivariate calibration (Table I, Table II, and Table III). The parameters for acceptance of this analysis were validated by the value of R^2 (coefficient determination) in calibration and validation, RMSEC, and RMSEP.

Table I. The comparation compilation of PCR and PLSR for quantitative analysis Jamu Pegel Linu (JPL) in ternary mixtures with prednisone and metamizole.

Multivariate calibrations	Wavenumber (cm^{-1})	Spectra	Calibration		Validation	
			R^2	RMSEC	R^2	RMSEP
PLSR	1636-682	normal	0.9928	4.00	0.9845	5.99
		derivative 1	0.9939	3.67	0.9857	5.80
		derivative 2	0.9934	3.81	0.9856	5.83
	3570-669	normal	0.9926	4.05	0.9861	5.71
		derivative 1	0.9919	4.22	0.9842	6.07
		derivative 2	0.9920	4.20	0.9846	6.00
	1436-736	normal	0.9933	3.84	0.9847	5.92
		derivative 1	0.9944	3.52	0.9861	5.71
		derivative 2	0.9939	3.67	0.9853	5.87
	1636-682 and 3570-669	normal	0.9928	3.98	0.9858	5.75
		derivative 1	0.9927	4.02	0.9848	5.96
		derivative 2	0.9926	4.05	0.9850	5.93
	1636-682 and 1436-736	normal	0.9930	3.92	0.9846	5.95
		derivative 1	0.9941	3.60	0.9859	5.76
		derivative 2	0.9936	3.75	0.9855	5.84
PCR	1636-682	normal	0.9988	1.61	0.9969	3.33
		derivative 1	0.9988	1.63	0.9976	2.89
		derivative 2	0.9985	3.44	0.9962	3.44
	3570-669	normal	0.9981	2.05	0.9943	3.96
		derivative 1	0.9980	2.12	0.9952	3.79
		derivative 2	0.9979	4.78	0.9915	4.78
	1436-736	normal	0.9978	2.23	0.9956	3.63
		derivative 1	**0.9991**	**1.44**	**0.9978**	**2.71**
		derivative 2	0.9993	1.27	0.9961	3.19
	1636-682 and 3570-669	normal	0.9983	1.95	0.9957	3.65
		derivative 1	0.9990	1.52	0.9968	3.23
		derivative 2	0.9988	1.62	0.9939	4.09
	1636-682 and 1436-736	normal	0.9977	2.24	0.9957	3.66
		derivative 1	0.9984	1.90	0.9968	3.19
		derivative 2	0.9983	1.91	0.9958	3.57

**the selected condition was marked with bold; PLSR = partial least square calibration; PCR = principle component regression; R^2 = coefficient of determination; RMSEC = Root Mean Square Error of Calibration; RMSEP = Root Mean Square Error of Prediction.

R^2 values performed the acceptance condition of parameters close to one and the lowest value of RMSEC and RMSEP. Discriminant Analysis used almost the whole region of wavenumber (3933-716cm^{-1}) for the classification model, and the result was evaluated by Coomans plot to find out the accuracy level.

RESULT AND DISCUSSION

The adulteration model using prednisone and metamizole in ternary mixture with pain reliever herbal medicine caused by the National Agency for Drug and Food report about the list of synthetic drugs commonly found in herbal medicine (Mustarichie *et al*., 2017). The PCA score plot in the previous study exhibited the different principal components (PCs) between unadulterated herbal medicine and drugs. Pain reliever herbal medicine contains several unique functional groups, including the OH group at 3288 cm^{-1}, the C=O functional groups at 1713 cm^{-1}, and the C-O group at 1018 cm^{-1} (Fatmarahmi *et al*., 2021). The multivariate calibrations optimization in ternary mixtures was carried out to select the optimum condition for building the best prediction model (Rohman *et al*., 2019).

Table II. The comparation compilation of PCR and PLSR for quantitative analysis Jamu Encok (JE) in ternary mixtures with prednisone and metamizole.

Multivariate calibrations	Wavenumber (cm^{-1})	Spectra	Calibration		Validation	
			R^2	RMSEC	R^2	RMSEP
PLSR	1636-682	normal	0.9956	3.12	0.9956	2.92
		derivative 1	0.9847	5.80	0.9792	7.05
		derivative 2	0.9834	6.03	0.9781	7.23
	3570-669	normal	0.9989	1.53	0.9951	3.59
		derivative 1	0.9801	6.61	0.9754	7.57
		derivative 2	0.9800	6.62	0.9754	7.57
	1436-736	normal	0.9962	2.90	0.9965	3.00
		derivative 1	0.9857	5.61	0.9797	6.96
		derivative 2	0.9839	5.95	0.9778	7.28
	1636-682 and 3570-669	normal	0.9990	1.52	0.9950	3.67
		derivative 1	0.9819	6.31	0.9769	7.36
		derivative 2	0.9814	6.39	0.9765	7.43
	1636-682 and 1436-736	normal	0.9959	3.02	0.9966	2.92
		derivative 1	0.9852	5.71	0.9794	7.01
		derivative 2	0.9837	5.99	0.9781	7.24
PCR	1636-682	normal	0.9987	1.66	0.9947	3.92
		derivative 1	0.9988	1.61	0.9960	3.20
		derivative 2	0.9992	1.29	0.9958	3.43
	3570-669	normal	0.9987	1.67	0.9949	3.69
		derivative 1	0.9987	1.67	0.9964	3.07
		derivative 2	0.9990	1.48	0.9937	4.18
	1436-736	normal	0.9985	1.79	0.9943	4.02
		derivative 1	0.9983	1.94	0.9961	3.22
		derivative 2	0.9988	1.61	0.9972	2.89
	1636-682 and 3570-669	normal	0.9988	1.64	0.9943	3.86
		derivative 1	0.9981	2.05	0.9957	3.47
		derivative 2	0.9990	1.51	0.9939	4.14
	1636-682 and 1436-736	normal	0.9987	1.71	0.9947	3.89
		derivative 1	0.9987	1.72	0.9960	3.24
		derivative 2	**0.9992**	**1.32**	**0.9957**	**3.41**

*the selected condition was marked with bold; PLSR = partial least square calibration; PCR = principle component regression; R^2 = coefficient of determination; RMSEC = Root Mean Square Error of Calibration; RMSEP = Root Mean Square Error of Prediction.

Multivariate calibration

PLSR, PCR, wavenumber region, and spectra type derivatization were performed to reveal the optimum state for quantitative analysis (Table I-III). The spectrum of samples obtained was divided into calibration and validation sets. The particular condition of ternary mixtures quantitative analysis was determined by the value of the coefficient of determination (R^2) close to one, the lowest values of RMSEC and RMSEP (Irnawati *et al*., 2019). The statistical parameters evaluated the accuracy model. Ternary mixtures model of prednisone and metamizole in JPL at first derivative 1436-736 cm^{-1} wavenumber region coupled with PCR was selected for quantitative analysis due to the optimal statistical parameter value. The values of R^2 calibration, RMSEC, R^2 prediction, and RMSEP were 0.9991, 1.44, 0.9978, and 2.71, respectively. JE's selected condition in ternary mixtures with prednisone, and metamizole was a combination of two wavenumber regions (1636-682and 1436-736) cm^{-1} using a second derivative coupled with PCR. The statistical parameter values were 0.9992, 1.32, 0.9957, and 3.41, subsequently for R^2 calibration, RMSEC, R^2 prediction, and RMSEP.

Table III. The comparation compilation of PCR and PLSR for quantitative analysis Jamu Sakit Pinggang (JSP) in ternary mixtures with prednisone and metamizole.

Multivariate calibrations	Wavenumber (cm^{-1})	Spectra	Calibration		Validation	
			R^2	RMSEC	R^2	RMSEP
PLSR	1636-682	normal	0.9939	3.68	0.9771	8.07
		derivative 1	0.9989	1.58	0.9974	2.43
		derivative 2	0.9887	5.00	0.9807	6.95
	3570-669	normal	0.9965	2.78	0.9922	4.96
		derivative 1	0.9988	1.60	0.9972	2.57
		derivative 2	0.9853	5.68	0.9774	7.47
	1436-736	normal	0.9923	4.11	0.9687	9.53
		derivative 1	0.9894	6.83	0.9811	6.83
		derivative 2	0.9897	4.77	0.9815	6.82
	1636-682 and 3570-669	normal	0.9947	3.41	0.9866	6.07
		derivative 1	0.9988	1.61	0.9972	2.57
		derivative 2	0.9867	5.41	0.9787	7.26
	1636-682 and 1436-736	normal	0.9934	3.82	0.9738	8.69
		derivative 1	0.9888	4.97	0.9806	6.94
		derivative 2	0.9891	4.89	0.9811	6.89
PCR	1636-682	normal	0.9981	2.04	0.9971	2.86
		derivative 1	**0.9989**	**1.57**	**0.9976**	**2.39**
		derivative 2	0.9991	1.39	0.9948	3.44
	3570-669	normal	0.9985	1.85	0.9974	2.80
		derivative 1	0.9989	1.59	0.9976	2.40
		derivative 2	0.9987	1.72	0.9944	3.72
	1436-736	normal	0.9983	1.94	0.9973	2.79
		derivative 1	0.9986	1.75	0.9973	2.60
		derivative 2	0.9990	1.47	0.9965	2.80
	1636-682 and 3570-669	normal	0.9985	1.83	0.9975	2.67
		derivative 1	0.9989	1.58	0.9976	2.40
		derivative 2	0.9989	1.53	0.9946	3.54
	1636-682 and 1436-736	normal	0.9982	2.01	0.9971	2.85
		derivative 1	0.9988	1.60	0.9976	2.41
		derivative 2	0.9991	1.44	0.9953	3.28

*

*the selected condition was marked with bold; PLSR = partial least square calibration; PCR = principle component regression; R^2 = coefficient of determination; RMSEC = Root Mean Square Error of Calibration; RMSEP = Root Mean Square Error of Prediction.

In addition, JSP in ternary mixtures with drugs was analyzed using PCR at wavenumber region of 1636-682 cm^{-1} and the value of R^2 calibration, RMSEC, R^2 prediction, and RMSEP were 0.9989, 1.57, 0.9976, and 2.39 respectively. The regression prediction curves between the actual (x-axis) and calculated (y-axis) of the ternary mixtures samples and the residual analysis (Figure 1, 2, and 3). Based on the evaluated result value of statistical parameters, the prediction models were acceptable in accuracy and precision.

The application of derivative spectra in this study could overcome the problem of overlapping peaks but decrease the sensitivity as a consequence (Riyanto *et al*., 2019). The selected parametrical value of multivariate calibration demonstrated an accurate and precise quantification when the high values of coefficient determination (R^2) in both calibration and prediction and low RMSEC and RMSEP value (Miller & Miller, 2010).

Discriminant analysis

Qualified as supervised pattern recognition technique, discriminant analysis (DA) can classify the unadulterated and adulterated pain reliever herbal medicine (Rohman *et al*., 2014).

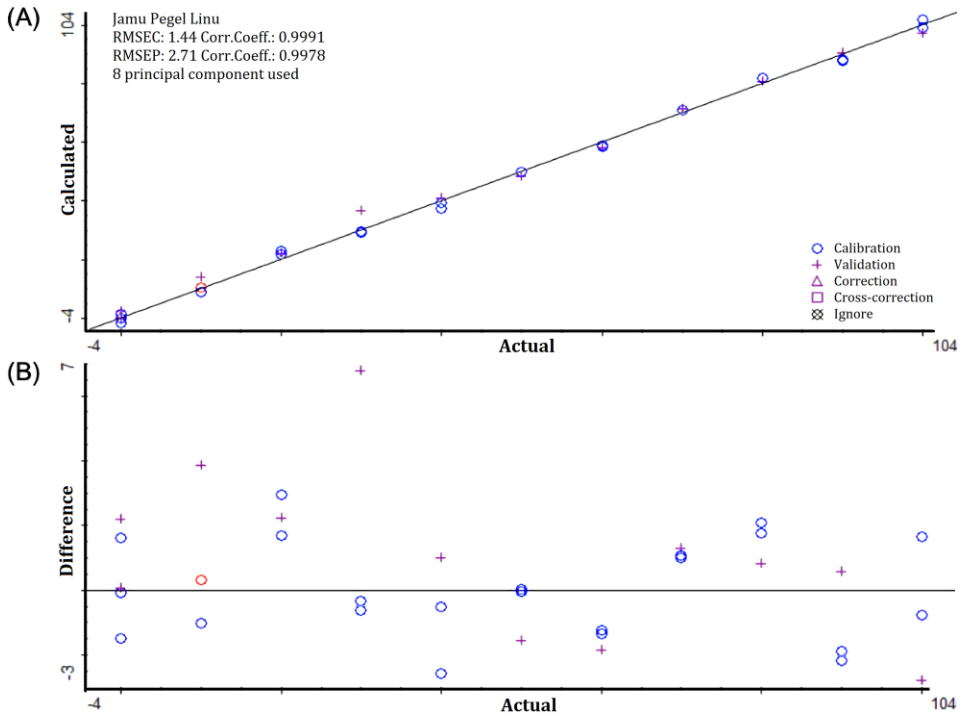

Figure 1. PCR models built training set for actual-predictions of Jamu Pegal Linu in ternary mixtures with prednisone and metamizole (A) along the residual analysis (B)

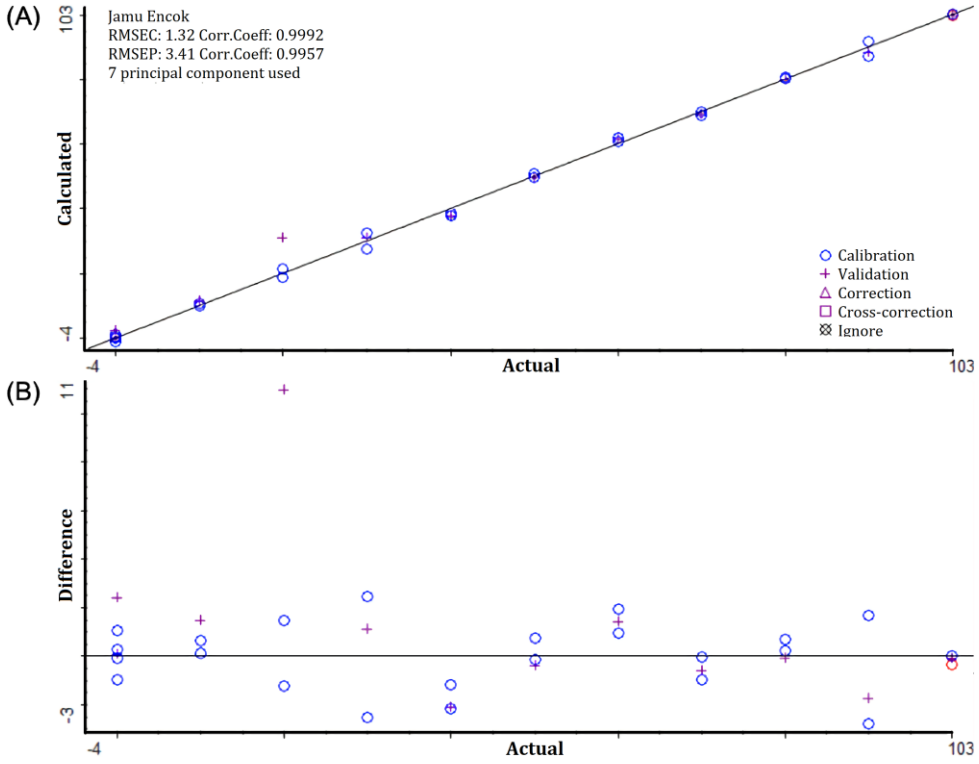

Figure 2. PCR models built in training set for the actual-predictions of Jamu Encok in ternary mixtures with prednisone and metamizole (A) along the residual analysis (B)

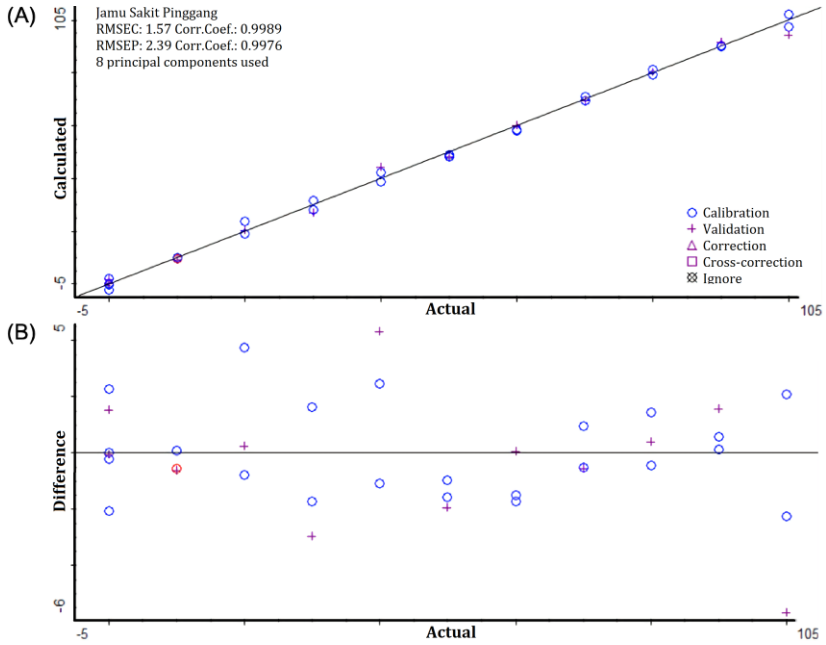

Figure 3. PCR models built training set for actual-predictions of Jamu Encok in ternary mixtures with prednisone and metamizole (A) along the residual analysis (B)

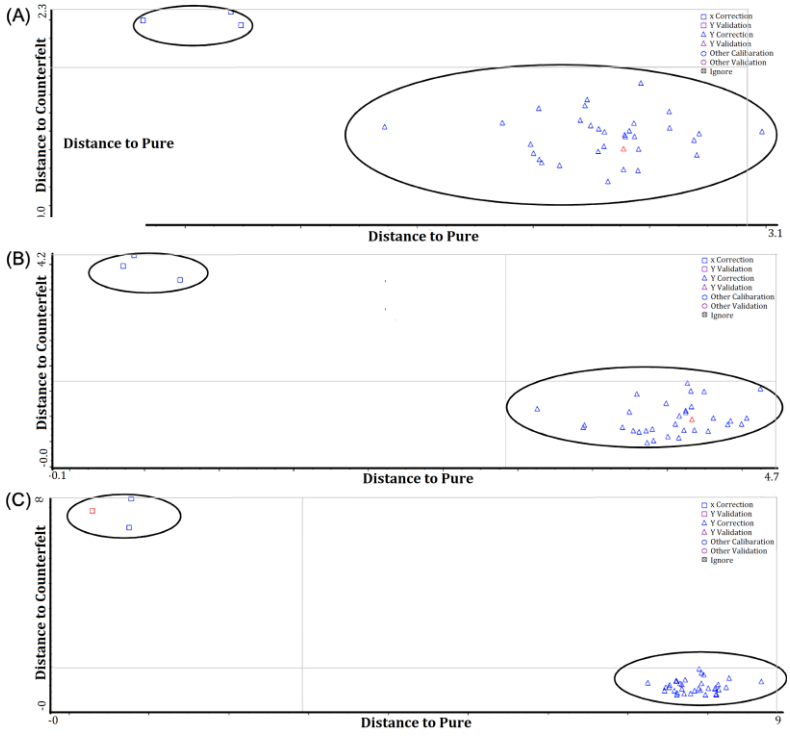

Figure 4. The Cooman's plot of discriminant analysis for discrimination between unadulterated herbal products (□) and ternary mixtures of samples (△). Jamu Pegal Linu (A), Jamu Encok (B), and Jamu Sakit Pinggang (C) in ternary mixtures with Prednisone and Metamizole

The Coomans Plot (Figures 4(A,B,C) revealed an accuracy level of 100% for categorizing prednisone and metamizole with pain reliever herbal medicine products using 3933-716cm^{-1} wavenumber region and calculation of Mahalanobis distance. This result represented the ability of DA to categorize pure herbal medicine from potential adulterants without any misclassification, especially synthetic drugs.

CONCLUSION

The combination of FTIR spectroscopy and multivariate calibrations (PLSR and PCR) also DA successfully quantified and classified the ternary mixtures between pain reliever herbal medicine products and prednisone and metamizole. This method could become effective and efficient in controlling the adulterated herbal products with synthetic drugs in the future.

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CONFLICT OF INTEREST

There is no conflict of interest declared.

REFERENCES

Al Lawati, H. A. J., Al Busaidi, I., Kadavilpparampu, A. M., & Suliman, F. O. (2017). Determination of Common Adulterants in Herbal Medicine and Food Samples using Core-shell Column Coupled to Tandem Mass Spectrometry. *Journal of Chromatographic Science*, *55*(3), 232–242. https://doi.org/10.1093/chromsci/bmw175

Ariffin, S. H., A Wahab, I., Hassan, Y., & Abd Wahab, M. S. (2021). Adulterated Traditional-Herbal Medicinal Products and Its Safety Signals in Malaysia. *Drug, Healthcare and Patient Safety*, *13*, 133–140. https://doi.org/10.2147/DHPS.S305953

Cebi, N., Yilmaz, M. T., & Sagdic, O. (2017). A rapid ATR-FTIR spectroscopic method for detection of sibutramine adulteration in tea and coffee based on hierarchical cluster and principal component analyses. *Food Chemistry*, *229*, 517–526. https://doi.org/10.1016/j.foodchem.2017.02.072

Ching, C. K., Chen, S. P. L., Lee, H. H. C., Lam, Y. H., Ng, S. W., Chen, M. L., Tang, M. H. Y., Chan, S. S. S., Ng, C. W. Y., Cheung, J. W. L., Chan, T. Y. C., Lau, N. K. C., Chong, Y. K., & Mak, T. W. L. (2018). Adulteration of proprietary Chinese medicines and health products with undeclared drugs: Experience of a tertiary toxicology laboratory in Hong Kong. *British Journal of Clinical Pharmacology*, *84*(1), 172–178. https://doi.org/10.1111/bcp.13420

Elfahmi, Woerdenbag, H. J., & Kayser, O. (2014). Jamu: Indonesian traditional herbal medicine towards rational phytopharmacological use. *Journal of Herbal Medicine*, *4*(2), 51–73. https://doi.org/10.1016/j.hermed.2014.01.002

Fatmarahmi, D. C., Susidarti, R. A., Swasono, R. T., & Rohman, A. (2021). Identification and Quantification of Metamizole in Traditional Herbal Medicines using Spectroscopy FTIR-ATR combined with Chemometrics. *Research Journal of Pharmacy and Technology*, *14*(8), 4413–4419.

Gitawati, R. (2013). Analisis Adulterasi Jamu Pegal Linu yang Diperoleh dari Pasar di Jakarta dan Sekitarnya (Analysis of Adulterated Jamu Pegal Linu Obtained from the Market in Jakarta). *Buletin Penelitian Sistem Kesehatan*, *16*(3 Jul). https://doi.org/10.22435/bpsk.v16i3Jul.3464

Irnawati, Riyanto, S., Martono, S., & Rohman, A. (2019). Determination of sesame oil, rice bran oil and pumpkin seed oil in ternary mixtures using FTIR spectroscopy and multivariate calibrations. *Food Research*, *4*(1), 135–142. https://doi.org/10.26656/fr.2017.4(1).260

Miller, J. N., & Miller, J. C. (2010). *Statistics and chemometrics for analytical chemistry* (6. ed). Prentice Hall.

Mustarichie, R., Ramdhani, D., & Indriyati, W. (2017). Analysis Of Forbidden Pharmaceutical Compouinds In Antirheumatic Jamu. *Asian Journal of Pharmaceutical and Clinical Research*, *10*(4), 98. https://doi.org/10.22159/ajpcr.2017.v10i4.16101

Riyanto, S., Martono, S., & Rohman, A. (2019). Analysis of palm oil as oil adulterant in olive and pumpkin seed oils in ternary mixture systems using FTIR spectroscopy and

chemometrics. *International Journal of Applied Pharmaceutics*, 210–215.

Rohman, A., Nugroho, A., Lukitaningsih, E., & Sudjadi. (2014). Application of Vibrational Spectroscopy in Combination with Chemometrics Techniques for Authentication of Herbal Medicine. *Applied Spectroscopy Reviews*, *49*(8), 603–613. https://doi.org/10.1080/05704928.2014.882347

Rohman, A., Windarsih, A., Hossain, M. A. M., Johan, M. R., Ali, M. E., & Fadzilah, N. A. (2019). Application of near- and mid-infrared spectroscopy combined with chemometrics for discrimination and authentication of herbal products: A review. *Journal of Applied Pharmaceutical Science*, *9*(3), 137–147. https://doi.org/10.7324/JAPS.2019.90319

Rooney, J. S., McDowell, A., Strachan, C. J., & Gordon, K. C. (2015). Evaluation of vibrational spectroscopic methods to identify and quantify multiple adulterants in herbal medicines. *Talanta*, *138*, 77–85. https://doi.org/10.1016/j.talanta.2015.02.016

Vaysse, J., Balayssac, S., Gilard, V., Desoubdzanne, D., Malet-Martino, M., & Martino, R. (2010). Analysis of adulterated herbal medicines and dietary supplements marketed for weight loss by DOSY ^{1}H-NMR. *Food Additives & Contaminants: Part A*, *27*(7), 903–916. https://doi.org/10.1080/19440041003705821