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The Giving Effects of Virgin Coconut Oil on Profile Pharmacokinetics Diclofenac Sodium

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Abstract : Pure coconut oil (*Virgin Coconut Oil*, VCO) includes medium chain fatty (*Medium Chain trigliseride*, MCT) is quickly digested and absorbed in a short time, can be converted into energy so as to increase the body's metabolism. It is thus able to influence the metabolism of drugs when combined with diclofenac sodium. The aim of this study is to determine the effect of VCO on the pharmacokinetics profile of diclofenac sodium. The method adopted in this study using Wistar rats of body weight 200-250 g. VCO used in this study is the Palm Mustika with variations of three doses of VCO (12.5 ml, 25 ml and 50 ml) and the therapeutic dose of diclofenac sodium (4.5 mg/kg). Span of blood samples (0', 15', 30', 45', 75', 105', 135', 195', 255', 315', 435') and the measurement of drug levels in the blood (K_{abs}, T_{max}, C_{max}, AUC, MRT AUMC, Vd, $T_{1/2}$, K_{el} and CL) using a High Performance Liquid Chromatography (HPLC). The result of data analysis is performed using one-way ANOVA. The results showed that the value K_{abs}, T_{max}, C_{max}, AUC, AUMC, MRT, Vd and $T_{1/2el}$ containing VCO with dose variation (12.5 ml, 25 ml, 50 ml) decreased compared to the control of diclofenac sodium. While the value of K_{el} and CL containing VCO with dose variation (12.5 ml, 25 ml, 50 ml) increased when compared to controls diclofenac sodium. This is because the VCO can increase the body's metabolism so that the effect on drug metabolism when combined with diclofenac sodium. While, according to statistics show that the value of K_{el} , $T_{1 / 2el}$, T_{max}, C_{max}, Vd and CL have a significance value < 0.05 which states that there are differences between groups . This is because the VCO influence to increase the body's metabolism so that if there are other chemicals into the body in this case sodium diclofenac will be quickly eliminated from the body.

Keywords: *Virgin Coconut Oil* (VCO),Pharmacokinetics, Diclofenac Soium, AntiInflammatory.

Introduction

Pure coconut oil (*Virgin Coconut Oil*, VCO) is known as a high lauric oils containing *Saturated Fatty Acids* together with glycerol to form *Medium Chain Triglycerides.* This oil is made from fresh coconut meat that is processed in a low temperature and without heating so that an essential ingredient in the oil can still be maintained. Virgin coconut oil has a clearer color and can hold stored for 2 years without becoming rancid[1].

According to the Official Website LPPI Chemical Research Center, the chemical content of VCO consists of 92 % *saturated fatty acids*, 6 % *monounsaturated fatty acids*, and 2 % *polyunsaturated fatty acids*. Chemical content in the form of a 64 % *saturated medium chain fatty acids* (MCFA) consists of more than 50 % *lauric acid* (C12:0), 6-7 % *capric acid* (C10:0), 8 % *caprylic acid* (C8:0), as well as some other types of fatty acids such as *myristic acid* (C14:0) and *palmitic acid* (C16:0)[2,3].

MCT in VCO is metabolized in the body in different ways with LCT. MCT solubility in water higher than LCT so MCT can enter the circulatory system, into the liver directly through the blood vessels (veins) and quickly burned into energy, which means MCT is not stored in tissues[4].

Diclofenac sodium is a phenyl acetic acid derivative with the chemical name sodium 2-[2- (2,6 diklorofenil) aminophenyl]-1-oksido-etanon or sodium {0-[(2,6 diklorofenil aminophenyl} acetate.This compound has the molecular formula $C_{14}H_{10}Cl_2NO_2Na$ molecular weight of 318.3. Diclofenac sodium is a derivative of a weak acid with a pKa of 4.2.Diclofenac sodium in the water will dissolve as Na^+ ion and anion diclofenac.

Diclofenac sodium in the short term use for acute conditions such as inflammatory pain in sprains, pain after dental surgery and a *nonsteroidal anti-inflammatory drug* (NSAID) which is commonly prescribed for the treatment of rheumatoid arthritis, osteoarthritis, musculoskeletal injuries, and postoperative analgesia in humans and animals. Patients are often given a special formulation of diclofenac as a therapeutic strategy[5,6].

Research on diclofenac sodium analysis using HPLC instrument has been done. Among the research which states that the determination of diclofenac sodium levels by optimizing the mobile phase solvent mixture akuabides with mobile phase asetonitril-0.01 M phosphate buffer pH 3.5 with a ratio of mobile phase (70:30) and the stationary phase octadecyl silicate C-18 at a flow rate of 1 ml/min[8]. Research states the assay of diclofenac sodium in rats conducted using a HPLC mobile phase of methanol-water (55:45), using a C-18 column at a flow rate of 1 ml / min[9].Assay of diclofenac sodium in plasma using a mobile phase HPLC trifluoroacetic acid-acetonitrile (65:35), column C-18 UV-VIS detector and a flow rate of 1 ml / min[5].

Other studies on the analysis of diclofenac sodium and paracetamol combined with klozoxason levels measured using a HPLC mobile phase phosphate buffer-acetonitrile-methanol (25:25:50) using TC-C18 column, flow rate of 1 ml/min. There are also studies analysis of diclofenac sodium and paracetamol combined with Methocarbamol HPLC using a mobile phase of methanol-water-GAA (400:600:05) flow rate of 1 ml / min[10].

Other studies claim that the analysis of diclofenac sodium using a mobile phase HPLC with methanol:acetate buffer (85:15) with a flow rate of 1 ml/min using TC-C18 column and a UV detector – Vis[7].

Their research on the analysis of diclofenac sodium combined with paracetamol HPLC using a mobile phase of acetonitrile:methanol (90:10) flow rate of 1 ml/min. There are also studies that serve as reference material for researchers using the same samples by previous researchers that diclofenac sodium as the main raw material and paracetamol as internal standard[11].

Based on the issues described above, researchers are interested to examine the possibility of the influence of *Virgin Coconut Oil* (VCO) on the profile the pharmacokinetics of diclofenac sodium.

Field Experiment and Sampling

Tools

The tools used are politube, glass beaker, vortex, water bath, centrifuge (Shimadzu), flask beakers, analytical balance (Beco Germany), pipette volume, gloves, stopwatch, mouse cage, mask, weighing animals, devices HPLC (Shimadzu), and other tools that are needed.

Materials

The materials used in this study is diclofenac sodium (Kimia Farma), Paracetamol (Mutifa), VCO (Palm Mustika), TCA 20 %, heparin (PT Pratapa Nirmala), akuabides (PT Ikapharmindo Putramas).

Research Procedure

a. Treatment Without Giving VCO

Animals in the form of Wistar rats that weigh ± 200-250 g the conditioned is given a suspension of diclofenac sodium, a blood sample from a vein lateral mice which lies on 10 points with a time interval that is

about 0', 15', 30', 45', 75', 105', 135', 195', 255', 315', 435' (adjusted for sampling). Blood is collected as much as 1 ml put in politube that has been given heparin, centrifuged at 3000 rpm for 10 minutes, clear liquid was taken and added to 1 ml of 20 % TCA vortex and sentrivuge 3000 rpm for 10 minutes and then taken a clear liquid.

b. Treatment With Giving VCO

Animals in the form of Wistar rats that weigh 200-250 g ± given VCO which has been conditioned for 28 days in a row[12]. On day twenty- eight after the VCO, 4 hours later granted a suspension of diclofenac sodium, a blood sample from a vein lateral mice which lies on 10 points with a time interval that is about 0 ', 15', 30', 45', 75 ', 105', 135 ', 195 ', 255 ', 315 ', 435 ' (adjusted for sampling). Blood is collected as much as 1 ml put in politube that has been given heparin, centrifuged at 3000 rpm for 10 minutes, clear liquid was taken and added to 1 ml of 20 % TCA vortex and sentrivuge 3000 rpm for 10 minutes and then taken a clear liquid[7].

Results and Discussion

From the measurement results of blood plasma levels obtained using HPLC instrument diclofenac sodium concentration values as shown in **Table 1** below.

Table 1. Values of Diclofenac Sodium Concentration in Plasma

Time (minutes)	Control of DiclofenacSodium (mcg/ml)	VCO 50 ml + DiclofenacSodium (mcg/ml)	VCO 25 ml + Diclofenac Sodium (mcg/ml)	VCO 12.5 ml + Diclofenak Sodium (mcg/ml)
15’	0.615±0.096	0.464±0.094	0.353±0.110	0.238±0.059
30’	0.770±0.099	0.630±0.079	0.489±0.095	0.425±0.128
45’	0.912±0.079	0.822±0.078	0.663±0.079	0.662±0.108
75’	1.683±0.256	1.017±0.150	0.925±0.097	0.900±0.136
105’	2.158±0.434	1.307±0.061	1.118±0.038	1.083±0.137
135’	1.444±0.385	1.008±0.106	0.888±0.119	0.909±0.114
195’	0.784±0.087	0.785±0.072	0.645±0.081	0.742±0.111
255’	0.558±0.102	0.555±0.113	0.449±0.074	0.532±0.062
315’	0.368±0.102	0.302±0.069	0.287±0.046	0.330±0.060
435’	0.177±0.073	0.187±0.064	0.177±0.069	0.143±0.056

From the data value of the average concentration of sodium diclofenac ± SD plasma above , it can be seen semilog table as shown in **Figure 1**.

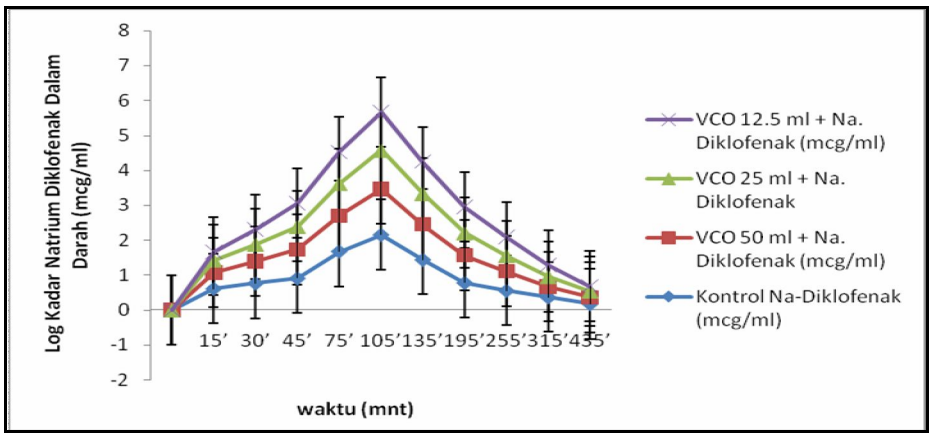

Figure 1. Graph Effect of VCO Against Drug Concentration In Blood VS Time

Based on the above concentrations can be determined pharmacokinetic profiles VCO towards the influence of diclofenac sodium. This is evident from the administration of the dose variation VCO (12.5 ml; 25 ml; 50 ml) in plasma compared to the control of diclofenac sodium that will generate value K_{abs}, T_{max}, C_{max}, AUC, AUMC, MRT, Vd, Kel, $T_{1/2}$ and CL. Such value can be seen in **Table 2**.

Table 2. Pharmacokinetics Parameter Value Diclofenac Sodium

Pharmacokinetics Parameter	Control of DiclofenacSodium	VCO 50 ml + DiclofenacSodium	VCO 25 ml + Diclofenac Sodium	VCO 12.5 ml + Diclofenak Sodium
Kabs (mnt^{-1})	0.027±0.003	0.022±0.007	0.0224±0.008	0.020±0.003
Tmaks (mnt)	98.08±13.59	92.2±9.71	86.55±6.2	78.68±7.83
Cmaks (mcg/ml)	1.59±0.23	0.99±0.13	0.75±0.06	0.68±0.14
$AUC_{0-\infty}$ (mcg/ml).mnt	13344.2±31814.8	283.29±31.15	260.78±39.3	254.8±24.3
$AUMC_{0-\infty}$ ($mcg/ml).mnt^2$	1428100.9±3336500	59100.1±17496.6	58756.1±16589.3	58027.3±12713.3
MRT (mnt)	227.6±43.5	223.3±29.4	203.2±23.5	170.4±37.1
Vd (ml)	1070669.1±168645.4	1022632.9±104842.9	894250.5±137083.1	468394.1±239092.9
Kel (mnt^{-1})	0.0049±0.0007	0.005±0.001	0.006±0.001	0.009±0.005
$T_{1/2\ el}$ (mnt)	145.15±22.72	128.9±30.5	106.4±17.9	84.0±28.5
CL (ml/mnt)	2590.3±1382.98	4453.3±872.7	4576.8±652.6	4882.2±1050.6

Data from the statistical analysis one-way ANOVA using SPSS 17 can be seen in **Table 3** below.

Table 3. Results of Data Analysis Using SPSS Statistics 17.

Parameter	Statistical Analysis Results	Information	Scheffe Test Results
Kabs (mnt^{-1})	0.261	p>0.05 (be accepted)	-
Tmaks (mnt)	0.016	p<0.05 (rejected)	A, B, C (0.270) B, C, D (0.157)
Cmaks (mcg/ml)	0.000	p<0.05 (rejected)	A (1.000) B, C (0.079) C, D (0.920)
$AUC_{0-\infty}$ (mcg/ml).mnt	0.407	p>0.05 (be accepted)	-
$AUMC_{0-\infty}$ ($mcg/ml).mnt^2$	0.409	p>0.05 (be accepted)	-
MRT (mnt)	0035	p<0.05 (rejected)	D, C, B, A (0.067)
Vd (ml)	0.000	p<0.05 (rejected)	D (1.000) C, B, A (0.381)
Kel (mnt^{-1})	0.050	p<0.05 (rejected)	A, B, C, D (0.076)
$T_{1/2\ el}$ (mnt)	0.003	p<0.05 (rejected)	C, B, A (0.105) D (0.521)
CL (ml/mnt)	0.004	p<0.05 (rejected)	A (1.000) B, C, D (0.921)

Discussion

From **Table 2** above shows that the value K_{abs}, T_{max}, C_{max}, AUC, AUMC, MRT, Vd and $T_{1/2el}$ containing VCO with dose variation (12.5 ml, 25 ml, 50 ml) decreased compared to control sodium diclofenac. While the value of K_{el} and CL containing VCO with dose variation (12.5 ml, 25 ml, 50 ml) increased when compared to controls diclofenac sodium. This is because the VCO can increase the body's metabolism so that the effect on drug metabolism when combined with diclofenac sodium.

Based on the results of statistical analysis of one-way ANOVA using SPSS 17 is shown in **Table 3** are values C_{max}, T_{max}, MRT, $T_{1/2el}$, K_{el}, Vd and CL have a significance value of $p < 0.05$.Stated that Ho is rejected. It can be concluded that there is a difference between the groups so that they can continue with advanced test that is Scheffe test. While the value of K_{abs}, $AUC_{0-\infty}$ and $AUMC_{0-\infty}$ has a significant value of $p > 0.05$. Stated that Ho is accepted . It was concluded that there were no differences between groups.

Conclusion

VCO affect the pharmacokinetic parameters of diclofenac sodium. VCO dose variation can affect the body's metabolism of diclofenac sodium compared with controls for their MCT is able to increase metabolism followed by increased content of cytochrome P-450 in liver microsomes. Increased cytochrome affect the metabolic rate of other chemicals. So if there are other chemicals that are in the body will be quickly eliminated.

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