

Kinetic and Thermodynamic Study of Extraction of Oleoresin Containing Curcuminoids from Turmeric (*Curcuma Longa* L.)

Anaclet B. Kunyima, Joseph C. Kuburhanwa, H  ritier M. Kaseya, Beno  t M. Mukendi, and Michel B. Kunyima

ABSTRACT

Numerous studies are nowadays undertaken across the world laboratories on turmeric and show its excellent virtues in various fields such as medicine, pharmacology, cosmetics, and so forth. In this paper, to enlarge the domain of scientific knowledge, a kinetic and thermodynamic behavior of curcuminoid extraction from *Curcuma longa* L has been investigated in the dilute medium using ethanol as solvent under a magnetic stirrer. Through the KUNYIMA method, by means of the KUNYIMA first law, the global kinetic constant has been calculated at 250 rounds per minute (rpm) and the data have shown its constance at 500 rounds per minute at the same temperature (27.5   C). The kinetic constant can serve to build a commercial tank of production of curcuminoids using the sizing factor to endow the Democratic Republic of the Congo with its home technology of curcuminoids extraction as is hereby discussed. Extraction enthalpy and entropy have been calculated in a closed system using the Arrhenius relation. The results of enthalpy indicate that the extraction of curcuminoids is an endothermic phenomenon. This endothermic behavior of the extraction of curcuminoids in ethanol under a magnetic stirrer probably suggests the predominance of the enol form of curcumin in presence of its tautomeric ketone form. Also, the extraction of curcuminoids in ethanol is an endothermic phenomenon and this last phenomenon probably suggests its non-bioavailability. The energy promoting solubilization of curcuminoids arises from the solvent, under a magnetic stirrer, that can meet its alike with the hydroxyl group (like dissolves like). The value of the variation of entropy has evidently suggested the disturbance of the natural order after extraction. Note that KUNYIMA's second law has been hereby announced.

Keywords: Enol Form, KUNYIMA First Law, KUNYIMA Second Law, Non-Bioavailability, Sizing Factor.

Published Online: July 24, 2022

ISSN: 2684-4478

DOI: 10.24018/ejchem.2022.3.2.107

A. B. Kunyima*

Laboratory of Physical Organic Chemistry, Food and Physical Cardiochemistry, Department of Chemistry and Industry, Faculty of Sciences, University of Kinshasa, Democratic Republic of the Congo.

(e-mail: anaclet.kunyima@unikin.ac.cd)

J. C. Kuburhanwa

University of Kinshasa, Kinshasa, Democratic Republic of the Congo.

(e-mail: kubchirjos@yahoo.fr)

H. M. Kaseya

University of Kinshasa, Kinshasa, Democratic Republic of the Congo.

(e-mail: kaseyaheritier2@gmail.com)

B. M. Mukendi

University of Kinshasa, Kinshasa, Democratic Republic of the Congo.

(e-mail: mukendib@gmail.com)

M. B. Kunyima

Higher Institute of Medical Techniques Hospital, Kinshasa/N'djili, Democratic Republic of the Congo.

(e-mail: michelkunyima75@gmail.com)

**Corresponding Author*

I. INTRODUCTION

Nowadays, much research performed in laboratories has shown interest in turmeric plants in diverse fields. Experimental studies have been intensified since 2002 on turmeric to understand its multiple mechanisms of action. Indeed, in 2002, Inano and Onoda studied the radioprotective action of curcumin extracted from turmeric *longa* Linn: inhibitory effect on the formation of urinary 8-hydroxy-20-deoxyguanosine, tumorigenesis, but not mortality, induced by gamma-ray irradiation [1].

In 2005, Reddy *et al.* published on curcumin for malaria therapy [2]. The same year, Notarbartolo *et al.* studied the antitumor effects of curcumin, alone or in combination with cisplatin or doxorubicin, on human hepatic cancer cells [3]. In 2006, Cui *et al.* published that curcumin inhibits telomerase activity in human cancer cell lines [4]. The same year Hong *et al.* published their work on the effects of curcumin on the invasiveness of prostate cancer in vitro and in vivo [5]. In 2007, di Mario *et al.* published an article on "A curcumin-based 1- week triple therapy for eradication of helicobacter pylori infection: something to learn from failure" [6]. The same year, John *et al.* talked about curcumin for chemoprevention of colon cancer [7], Kowluru *et al.* studied the effects of curcumin on retinal oxidative stress and inflammation in diabetes [8], Li *et al.* published "Curcumin, a dietary component, has anticancer, chemosensitization, and radiosensitization effects by down-regulating the MDM2 oncogene through the PI3K/mTOR/ETS2 pathway" [9]. In 2008, it was the turn of Gaurisankar *et al.* in Anti-cancer effects of curcumin: the cycle of life and death [10]. The same year, Patel *et al.* published "Curcumin enhances the effects of 5-fluorouracil

and oxaliplatin in mediating growth inhibition of colon cancer cells by modulating EGFR and IGF-IR” [11]. In 2014, Li *et al.* published on the chemopreventive activity of turmeric essential oil and possible mechanisms of action [12]. In 2015, Zhou *et al.* studied the essential oil of curcuma Wenyujin, which inhibits osteogenic differentiation in ankylosing spondylitis [13]. In 2022, Kunyima *et al.* published an article on “Anti-myocardial infarctus, efficient anti-poison and anti-prostate mighty spicy miscellany” [14]. The list is not exhaustive. The turmeric studies revealed that curcuminoids would prevent cancers (colon, lung, prostate, kidney, liver, skin, stomach, leukemia, oesophagus, etc.) and may contribute to their treatment. Turmeric treats stomach ulcers and inflammatory diseases (rheumatoid arthritis), relieves liver troubles, reduces hyperlipidemia and the risk of cardiovascular diseases; treats gingivitis (gum disease), prevents diabetes of type 2, and decreases the inflammation among diabetic patients suffering from nephropathy. Turmeric would improve the cognition performance in Alzheimer's patients (research is going on). The inflammation of the skin and wounds can be also treated with turmeric. In a recent publication [14] Kunyima *et al.* showed the healing power of spicy miscellany based on turmeric. We are convinced that many things remain unknown about curcuminoids despite abundant literature.

II. MATERIALS AND METHODS

A. Materials

Ethanol 96 % has been used as a solvent.

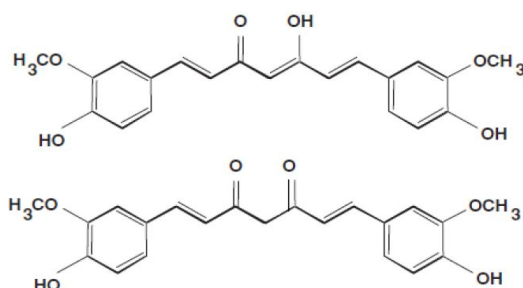


Fig. 1: Chemical structures of curcumin (enol and keto).

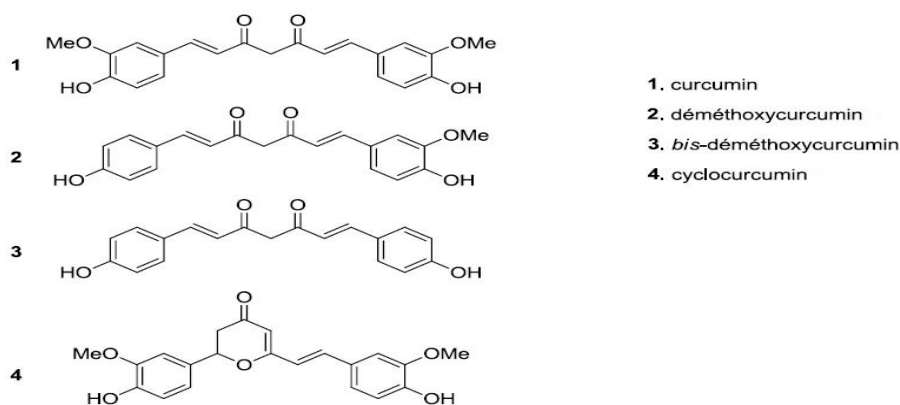


Fig. 2: Structure of curcuminoids.

B. Methods

1) KUNYIMA Method, KUNYIMA First Law and KUNYIMA Second Law

KUNYIMA method is a reasoning procedure consisting of apprehending a phenomenon, to try to mathematize it which means to express it in a mathematical equation. This equation is then solved, and the solution is tested by experimental. When this solution is verified by experiments, it becomes a law. In the case under study that means the extraction of curcuminoids in ethanol as solvent, it can be done massic balance sheet. Indeed the instantaneous variation of quantity is equal to the inlet massic debit of curcuminoids in turmeric minus the exit massic debit of curcuminoids from turmeric [15]. This corresponds to Equation (1).

$$\frac{dx_i}{dt} = \sum_{j=1}^n k_{ij}x_j - \sum_{j=1}^n k_{ji}x_i \quad (1)$$

To understand (1), it may imagine the quantity of oleoresin containing curcuminoids entering the turmeric (i) represented by the first term and the quantity of oleoresin leaving the turmeric towards solvent (j) represented by the second term. The first term is zero, the extraction begins with the total quantity of oleoresin containing curcuminoids already formed inside turmeric. There is no entrance. There is only the exit of oleoresin by extraction. This corresponds to Equation (2).

$$\frac{dx_i}{dt} = \sum_{\substack{j=1 \\ j \neq i}}^n k_{ij} x_i \quad (2)$$

k_{ij} is the kinetic constant when the oleoresin containing curcuminoids leaves the solid state (i) towards ethanol (j) as a solvent and for the rest, it will be written only k . Considering the oleoresin containing curcuminoids as a unique compound, the addition sign (Σ) disappears.

$$m = m_t = m_0 = x \quad (3)$$

m_0 : is the extractable mass of oleoresin containing curcuminoids in ethanol in (gr)
 m_0 : depends on the polarity of the solvent, its polarizability, its refractive index (properties of solvent)
 x : is the conversion (extracted mass of oleoresin containing curcuminoids at time t)

$$x = x_t = m_0 - m \quad (4)$$

m_0 : is considered as a constant in each solvent and at a given temperature.

$$\frac{dx_i}{dt} = -\frac{dm}{dt} = k(m_0 - x) \quad (5)$$

$$\int \frac{dx_i}{m_0 - x} = \int k dt \quad (6)$$

$$-\ln(m_0 - x) = kt + \ln B \quad (7)$$

At $t = 0$, $x = 0$

$$-\ln m_0 = \ln B \quad (8)$$

$$-\ln(m_0 - x) = kt - \ln m_0 \quad (9)$$

$$\ln m_0 - \ln(m_0 - x) = kt \quad (10)$$

$$\ln\left(\frac{m_0}{m_0 - x}\right) = kt \quad (11)$$

$$\log\left(\frac{m_0}{m_0 - x}\right) = \frac{k}{2.3} t = \log\left(\frac{1}{m_0 - x}\right) = \frac{k}{2.3} t + \log \frac{1}{m_0} \quad (12)$$

Equation (12) is the work equation. For the rest, we use: $x = m_e$

Thus, Equation (12) becomes Equation (13). KUNYIMA method allows us to establish (13).

$$\log\left(\frac{m_0}{m_0 - m_e}\right) = \frac{k}{2.3} t \quad (13)$$

Now (13) should be tested by experiments. When we plot (13) vs time, we should obtain a straight line whose slope gives us $\frac{k}{2.3}$ as there is no intercept here. When the second form of (12) is used, the intercept is $\frac{1}{m_0}$. This equation established by the KUNYIMA method becomes law because it has been verified by experiments as follows.

Indeed, (13) has been successfully tested by experiments in the case of extraction of Gourd seeds oil [16], Moringa seeds oil [17], Sesame seeds oil [18], and now in the extraction of oleoresin-containing curcuminoids from Turmeric in ethanol. It is the reason why the laboratory has decided to call it KUNYIMA first law, to honor Dr. Anacleto Kunyima Badibanga, chairman of Lacopa-PCC, who gave this elegant tool to undertake the extraction studies in a dilute medium.

Now it becomes possible for researchers to undertake a kinetic and thermodynamic study of the extraction [19] as it will be likewise shown in this paper in the case of extraction of oleoresin containing curcuminoids in ethanol.

KUNYIMA's first law can take the following form:

$$x = m_e = m_0(1 - e^{-kt}) \quad (14)$$

$$x = m_e = m_0 - m_0 e^{-kt} \quad (15)$$

m_0 is constant.

$$m_0 - m_e = m_0 e^{-kt} \quad (16)$$

$$e^{-kt} = \frac{m_0 - m_e}{m_0}$$

$$v = \frac{dx}{dt} = km_0 e^{-kt} = \frac{km_0(m_0 - m_e)}{m_e} \quad (17)$$

$$v = \frac{dx}{dt} = k(m_0 - m_e) \quad (18)$$

Where v is the extraction velocity or massic velocity (massic debit) in $\frac{g}{s}, \frac{g}{min}, \frac{g}{h}$ depending on the expression of time used in the experiment. It is the equivalent of F . In the case in the study extraction velocity will be expressed in $\frac{g}{min}$ because the stirring time is expressed in minutes.

For the study in title, k is the global kinetic constant of oleoresin and all the curcuminoids. It will be expressed in (s^{-1}), (min^{-1}), and (h^{-1}) if the extraction time is in second, in a minute, or in hours.

If the extraction concerns a compound of well-defined chemical structure, KUNYIMA's first law can be written in a concentration expressed in molarity. It becomes KUNYIMA's second law. That means:

$$\log\left(\frac{C_0}{C_0 - C_e}\right) = \frac{k}{2.3} t \quad (19)$$

C_0 = extractable concentration in $\frac{mol}{l}$ in solvent

C_e = extracted concentration $\frac{mol}{l}$ at time t .

KUNYIMA second law has been successfully also tested in the case of curcumin as it will be shown in the next publication. This second law can take the form (20).

$$C_e = C_0(1 - e^{-kt}) \quad (20)$$

2) Determination of the Volume of Extraction Reactor V_r by Means of Kinetic Constant k and Conversion Rate γ : Sizing Factor

In this paragraph, we want to solve the timeless problem of the transfer of technology and endow the country with its' home technology. The volume of the extraction reactor depends on the desired quantity of materials it is needed to be produced. It is shown below how to build an extraction reactor knowing kinetic constant k and conversion rate (γ). The chosen example concerns the determination of the volume of a closed continuous stirrer pilot tank (reactor) from kinetic constant (k) and conversion rate (γ).

The mass balance of a reactant can be written in a general form applicable to all types of reactors. For a time element dt and a volume element dv , the general form is shown in Equation (21).

$$\{\text{Mass of reactant entering volume element}\} - \{\text{Mass of reactant leaving volume element}\} - \{\text{Mass of reactant converted into volume element}\} = \{\text{Emphasis of reactant into volume element}\} \quad (21)$$

The first 2 terms represent the mass of reactants entering and leaving the reactor during time dt . The 3rd term depends on the rate of the reaction (interaction) applicable in the volume element dv . The 4th term expresses the resulting change in mass of reactants during the time dt caused by the 3 other terms. The 3rd term can be of the form $\Gamma \cdot V \cdot \Delta t$ where Γ represents the rate of disappearance of the reactant per unit volume.

Consider the simple case where there is a feed flow and a product flow. The properties of these flows do not change with time. The 1st and the 2nd term of the above equation of mass balance are constant and are equal to the flow velocity of the masses of reactants multiplied by dt . Remember that there is only interaction.

Let F be the mass flow rate of the reactants and γ_F the conversion to feed. The mass of reactant entering the reactor is shown in Equation (22).

$$F\Delta t - F\gamma_F\Delta t = F(1 - \gamma_F)\Delta t \quad (22)$$

The mass of reactant leaving the reactant volume element is shown in Equation (23)

$$F\Delta t - F\gamma_E\Delta t = F(1 - \gamma_E)\Delta t \quad (23)$$

where γ_E is the conversion at the output. As the reaction (interaction) of the mixture is at uniform temperature and composition, the reaction (interaction) rate is constant and can be evaluated at the temperature and composition of the product. Let Γ be the reactant conversion rate.

The mass of reactant converted into a product will be $\Gamma V \Delta t$. Assuming there is no buildup of reactant mass in the reactor, the equation of mass balance becomes:

$$F(1 - \gamma_F)\Delta t - F(1 - \gamma_E)\Delta t - \Gamma V \Delta t = 0 \quad (24)$$

$$F(1 - \gamma_F) - F(1 - \gamma_E) - \Gamma V = 0 \quad (25)$$

$$F(1 - \gamma_F) - F(1 - \gamma_E) = \Gamma V \quad (26)$$

$$F - \gamma_F F - F + \gamma_E F = \Gamma V \quad (27)$$

$$F(\gamma_E - \gamma_F) = \Gamma V \quad (28)$$

$$\frac{V}{F} = \frac{(\gamma_E - \gamma_F)}{\Gamma} = \frac{\gamma}{\Gamma} \quad (29)$$

This expression can be used to estimate the volume of the reactor required to produce a given conversion γ_E and to know the conditions F and γ_F . The reaction (interaction) rate is constant in the reactor. To evaluate Γ it is necessary to know the temperature of the product.

$$F = \frac{\text{mass}}{\text{time}} \quad (\text{massic velocity or massic debit})$$

Γ = extraction velocity (interaction velocity per unit of volume or massic velocity per volume)

$$\gamma = \frac{C_0 - C}{C_0} \quad (30)$$

$$F = QC_0 \quad (31)$$

Where $[C_0] = \frac{F}{Q} = \frac{\text{mass}}{\text{volume}}$ and C_0 is the feeding concentration.

$$\frac{V_r}{QC_0} = \frac{C_0 - C}{\Gamma C_0} \quad (32)$$

$$\bar{\theta} = \frac{V_r}{Q} = \frac{C_0 - C}{\Gamma} \quad (33)$$

$\bar{\theta}$ is the mean dwelling time (mean stay time) of materials in the reactor. Q is the volumic velocity (volumic debit).

$$\Gamma = kC \Rightarrow \Gamma = kC_0(1 - \gamma) \quad (34)$$

$$\bar{\theta} = \frac{V_r}{Q} = \frac{C_0 - C}{kC} \quad (35)$$

$$C = C_0 - \gamma C_0 \Rightarrow \gamma C_0 = C_0 - C \quad (36)$$

$$\bar{\theta} = \frac{V_r}{Q} = \frac{C_0 - C}{k C_0 (1 - \gamma)} \quad (37)$$

$$\bar{\theta} = \frac{V_r}{Q} = \frac{\gamma C_0}{k C_0 (1 - \gamma)} \quad (38)$$

$$\bar{\theta} = \frac{V_r}{Q} = \frac{\gamma}{k(1 - \gamma)} \quad (39)$$

$$V_r = \frac{\gamma}{k(1 - \gamma)} Q \quad (40)$$

$$A = \frac{\gamma}{k(1 - \gamma)} \quad (41)$$

$$V_r = A Q \quad (42)$$

A has been called the sizing factor. If the sizing factor and the desired volumic debit (Q) are known the minimum volume of the reactor V_r can be determined. Now the specialists can give the desired form to the reactor by determining its diameter, its length if it has a regular form. The reactor must work at the same temperature where k has been determined and in a similar environment. γ can be determined in the following way:

$$\bar{\theta} = \frac{V_r}{Q} = \frac{C_0 - C}{\Gamma} \text{ with } \Gamma = kC \quad (43)$$

$$\frac{V_r}{Q} = \frac{C_0 - C}{kC} \Rightarrow C = \frac{C_0}{1 + k\left(\frac{V_r}{Q}\right)} \quad (44)$$

$$C = \frac{C_0}{1 + k\theta} \quad (45)$$

$$\gamma = \frac{C_0 - C}{C_0} = 1 - \frac{C}{C_0} = 1 - \frac{1}{1 + k\theta} = \frac{k\theta}{1 + k\theta} \quad (46)$$

3) Thermodynamic study of curcuminoids

The global kinetic constant of oleoresin containing curcuminoids is determined in a closed system, the Arrhenius relation can be used to assess the values of extraction enthalpy and extraction entropy.

$$k = A' e^{-E/RT} \quad (47)$$

$$\ln k = \ln A' - \frac{E}{RT} \quad (48)$$

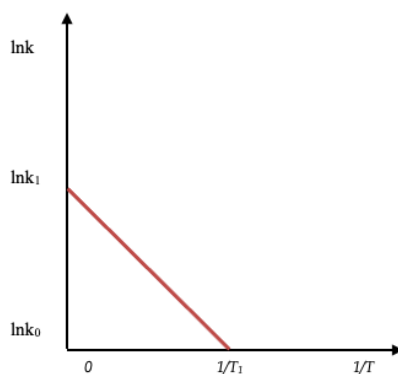


Fig. 3: $\ln k$ versus $\frac{1}{T}$.

$$\text{slope} = \frac{\ln k_1 - \ln k_0}{\frac{1}{T_1} - 0} = -\frac{E}{R} \quad (49)$$

In which $\ln k_0 = 0$

$$\text{slope} = \frac{\ln k_1}{\frac{1}{T_1}} = -\frac{E}{R} \quad (50)$$

$$-E = RT_1 \ln k_1 \quad (51)$$

$$E = -RT \ln k \quad (52)$$

The experiments have been performed in a closed system at temperature and pressure constant.

$$dG = -SdT + VdP \rightarrow \Delta G = 0 \quad (53)$$

$$dH = +TdS + VdP \rightarrow \int dH = \int TdS \quad (54)$$

$$\Delta H = T\Delta S \quad (55)$$

$$\Delta S = \frac{\Delta H}{T} \quad (56)$$

The energy calculated is $\Delta H = E$

$$\Delta H = E = -RT \ln k \quad (57)$$

4) Extraction protocol

Natural turmeric rhizomes have been bought at the Kinshasa market, dried at 50 °C, and afterward ground. One gram of turmeric powder has been placed in the cartridge. This cartridge has been placed in a flat bottom balloon flask containing a magnetic stirrer and 100 ml of ethanol as solvent. The thermometer has been placed in a balloon flask orifice to control the temperature that must be constant during all the experiments (27.5 °C) in the lee of light. The balloon flask endowed with a magnetic stirrer with its content has been placed on a heating agitator to be stirred at 250 rpm during a certain time. At each stirring time, the solvent (ethanol) has been removed from the mixture by means of a spin evaporator (mark Hei-VAP 1.0) programmed at 79 °C for ethanol for 20 minutes at 80 rpm. Afterward, the balloon flask has been placed in a drying oven at 80 °C for 10 minutes and cooled in a desiccator before being weighed in order to determine the extracted mass of oleoresin-containing curcuminoids. At each stirring time, the experiment has been repeated in exactly the same condition. The experiment has been also performed at 500 rpm.

III. RESULTS AND DISCUSSION

As it is shown in Table I (likewise for the following tables) each value of the extracted mass of oleoresin containing curcuminoids at 27.5 °C and 250 rpm is a mean value of three measures, the mean error has been used to express the precision of the measures. The precision (Δm_e) on the difference ($m_o - m_e$) has been calculated by the logarithmic method with m_o constant. Likewise, the precision of the massic velocity (Table II and Table IV) has been calculated by the logarithmic method considering m_o and k constants. Assuming that the extraction of turmeric rhizomes by ethanol or acetone gives 6 - 10% of oleoresin containing 35-45 % of curcuminoids [20] and these latters are responsible of turmeric's characteristic yellow-orange color while the essential oil contributes to its aroma and its typical flavor [21], it is shown in Table I the evolution of extracted mass (m_e) of oleoresin containing curcuminoids as a function of stirring time expressed in minutes at 27.5 °C with the magnetic stirrer velocity of 250 rpm. It can be seen in this table that the extracted mass of oleoresin-containing curcuminoids increases in ethanol when the stirring time increases until it reaches the maximum at 60 minutes of stirring time after which it remains quasi-constant whatever stirring time as it is indicated in Fig. 4.

At that point of the beginning of constant appearance the total extracted mass of oleoresin containing curcuminoids (m_o) in ethanol can be determined. The value of m_o in this table is (0.3670 ± 0.0004) gr.

Using KUNYIMA's first law which means plotting $\log \left(\frac{m_o}{m_o - m_e} \right)$ versus stirring time the kinetic constant can be determined as can be observed in Fig. 5.

TABLE I: EXTRACTED MASS OF OLEORESIN CONTAINING CURCUMINOIDS AS A FUNCTION OF STIRRING TIME AT 27.5 °C (250 RPM)

Temps (min)	m_e (gr)	m_o (gr)	$m_o - m_e$	$\frac{m_o}{m_o - m_e}$	$\log \frac{m_o}{m_o - m_e}$
0	0	0.3670 ± 0.0004	0.3670 ± 0.0004	1	0
1	0.0534 ± 0.0002	0.3670 ± 0.0004	0.3136 ± 0.0002	1.1705	0.0684
3	0.1381 ± 0.0004	0.3670 ± 0.0004	0.2289 ± 0.0004	1.6035	0.2051
6	0.2243 ± 0.0002	0.3670 ± 0.0004	0.1427 ± 0.0002	2.5713	0.4102
9	0.2779 ± 0.0003	0.3670 ± 0.0004	0.0890 ± 0.0003	4.1231	0.6152
12	0.3115 ± 0.0005	0.3670 ± 0.0004	0.0555 ± 0.0005	6.6114	0.8203
15	0.3324 ± 0.0004	0.3670 ± 0.0004	0.0346 ± 0.0004	10.6008	1.0253
18	0.3454 ± 0.0004	0.3670 ± 0.0004	0.0216 ± 0.0004	16.9986	1.2304
20	0.3512 ± 0.0004	0.3670 ± 0.0004	0.0158 ± 0.0004	23.2868	1.3671
23	0.3571 ± 0.0005	0.3670 ± 0.0004	0.0098 ± 0.0005	37.3349	1.5721
26	0.3609 ± 0.0003	0.3670 ± 0.0004	0.0061 ± 0.0003	59.8695	1.7772
29	0.3632 ± 0.0002	0.3670 ± 0.0004	0.0038 ± 0.0002	96.0733	1.9826
33	0.3649 ± 0.0005	0.3670 ± 0.0004	0.0021 ± 0.0005	174.7619	2.2424
36	0.3657 ± 0.0004	0.3670 ± 0.0004	0.0013 ± 0.0004	288.7764	2.4606
40	0.3663 ± 0.0003	0.3670 ± 0.0004	0.0007 ± 0.0003	539.7059	2.7322
45	0.3667 ± 0.0004	0.3670 ± 0.0004	0.0003 ± 0.0004	1223.3333	3.0875
50	0.3669 ± 0.0003	0.3670 ± 0.0004	0.0001 ± 0.0003	3670	3.5647
60	0.3670 ± 0.0004	0.3670 ± 0.0004	0	-	-

TABLE II: MASSIC VELOCITY (v) AS A FUNCTION OF EXTRACTED MASS OF OLEORESIN CONTAINING CURCUMINOIDS (m_e) AT 250

Temps (min)	m_e (gr)	m_o (gr)	$m_o - m_e$	k (min ⁻¹)	v (gr.min ⁻¹)
0	0	0.3670±0.0004	0.3670±0.0004	0.1597±0.0012	0.05860*±0.00000
1	0.0534±0.0002	0.3670±0.0004	0.3136±0.0002	0.1597±0.0012	0.05010±0.00003
3	0.1381±0.0004	0.3670±0.0004	0.2289±0.0004	0.1597±0.0012	0.03660 ±0.00006
6	0.2243±0.0002	0.3670±0.0004	0.1427±0.0002	0.1597±0.0012	0.02280±0.00003
9	0.2779±0.0003	0.3670±0.0004	0.0890±0.0003	0.1597±0.0012	0.01420±0.00048
12	0.3115±0.0005	0.3670±0.0004	0.0555±0.0005	0.1597±0.0012	0.00880±0.00008
15	0.3324±0.0004	0.3670±0.0004	0.0346±0.0004	0.1597±0.0012	0.00550±0.00006
18	0.3454±0.0004	0.3670±0.0004	0.0216±0.0004	0.1597±0.0012	0.00340±0.00063
20	0.3512±0.0004	0.3670±0.0004	0.0158±0.0004	0.1597±0.0012	0.00250±0.00006
23	0.3571±0.0005	0.3670±0.0004	0.0098±0.0005	0.1597±0.0012	0.00160±0.00008
26	0.3609±0.0003	0.3670±0.0004	0.0061±0.0003	0.1597±0.0012	0.00100±0.00005
29	0.3632±0.0002	0.3670±0.0004	0.0038±0.0002	0.1597±0.0012	0.00060±0.00003
33	0.3649±0.0005	0.3670±0.0004	0.0021±0.0005	0.1597±0.0012	0.00030±0.00007
36	0.3657±0.0004	0.3670±0.0004	0.0013±0.0004	0.1597±0.0012	0.00020±0.00006
40	0.3663±0.0003	0.3670±0.0004	0.0007±0.0003	0.1597±0.0012	0.00010±0.00004
45	0.3667±0.0004	0.3670±0.0004	0.0003±0.0004	0.1597±0.0012	0.00005±0.00007
50	0.3669±0.0003	0.3670±0.0004	0.0001±0.0003	0.1597±0.0012	0.00002±0.00008
60	0.3670±0.0004	0.3670±0.0004	0	0.1597±0.0012	0

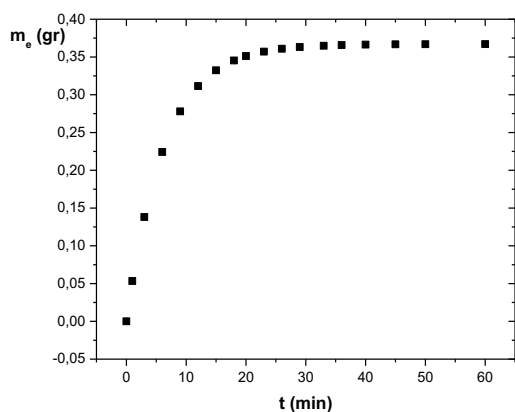


Fig. 4: Extracted mass (m_e) of oleoresin containing curcuminoids versus stirring time at 250 rpm.

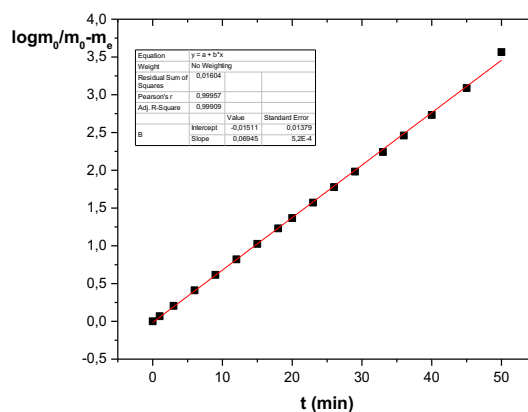


Fig. 5: $\log \left(\frac{m_o}{m_o - m_e} \right)$ versus stirring time at 250 rpm.

According to the Origin Program 9.2, the value of the global kinetic constant has been assessed at $(0.1597 \pm 0, 0012) \text{ min}^{-1}$ in the above-evoked work conditions. This global kinetic constant suggests the facility with which the oleoresin with its content is extracted by ethanol, it is somewhat a measure of solubility of the curcuminoids in ethanol.

Table II gives the evolution of massic velocity as a function of extracted mass (m_e) of oleoresin-containing curcuminoids at 27.5 °C (250 rpm). In Table II, the evolution of massic velocity (v) with the increase of extracted mass of oleoresin with its content (m_e) in ethanol can be observed.

The decrease of massic velocity has been evidenced without surprise at 27.5 °C in accordance with (18), suggesting the ethanol saturation in curcuminoids for a given sample as it is shown in Fig. 6.

The experiments have been also performed at 500 rpm as it is shown in Table III. Table III shows the evolution of the extracted mass of oleoresin with its content in ethanol as a function of stirring time maintaining temperature constant and the closed environment constant except for the magnetic stirrer velocity now at 500 rpm. It can be observed in this table the increase of extracted mass of curcuminoids at each stirring time until it remains constant to allow the calculation of m_o found to be (0.4515 ± 0.0003) gr as indicated in Fig. 7.

Applying KUNYIMA's first law the global kinetic constant has been found practically the same as it can be seen in Fig. 8 ($k = 0, 1597 \pm 0, 0001$) min^{-1} .

This result suggests that the global kinetic constant of extraction of oleoresin-containing curcuminoids in ethanol depends on temperature and environment. When the temperature is kept constant and in a given solvent, the global kinetic constant remains constant. The same kinetic constant has been found. Mass velocity has been also investigated at 500 rpm as indicated in Table IV.

TABLE III: EXTRACTED MASS OF OLEORESIN CONTAINING CURCUMINOIDS AS A FUNCTION OF STIRRING TIME AT 27.5 °C (500 RPM)

Temps (min)	m_e (gr)	m_o (gr)	$m_o - m_e$	$\frac{m_o}{m_o - m_e}$	$\log \frac{m_o}{m_o - m_e}$
0	0	0.4515 ± 0.0003	0.4515 ± 0.0003	1	0
1	0.0666 ± 0.0004	0.4515 ± 0.0003	0.3849 ± 0.0004	1.1731	0.0694
3	0.1619 ± 0.0005	0.4515 ± 0.0003	0.2896 ± 0.0005	1.6146	0.2081
6	0.2783 ± 0.0003	0.4515 ± 0.0003	0.1732 ± 0.0003	2.6070	0.4161
9	0.3442 ± 0.0006	0.4515 ± 0.0003	0.1073 ± 0.0006	4.2090	0.6224
12	0.3851 ± 0.0003	0.4515 ± 0.0003	0.0664 ± 0.0003	6.7966	0.8223
15	0.4104 ± 0.0004	0.4515 ± 0.0003	0.0414 ± 0.0004	10.6720	1.0403
18	0.4260 ± 0.0004	0.4515 ± 0.0003	0.0255 ± 0.0004	17.7198	1.2484
20	0.4330 ± 0.0006	0.4515 ± 0.0003	0.0185 ± 0.0006	24.3790	1.3870
23	0.4400 ± 0.0005	0.4515 ± 0.0003	0.0115 ± 0.0005	39.3636	1.5951
26	0.4446 ± 0.0004	0.4515 ± 0.0003	0.0069 ± 0.0004	65.3401	1.8152
29	0.4471 ± 0.0005	0.4515 ± 0.0003	0.0044 ± 0.0005	102.6136	2.0112
33	0.4492 ± 0.0006	0.4515 ± 0.0003	0.0023 ± 0.0006	194.6121	2.2892
36	0.4501 ± 0.0003	0.4515 ± 0.0003	0.0014 ± 0.0003	313.5417	2.4963
40	0.4507 ± 0.0005	0.4515 ± 0.0003	0.0008 ± 0.0005	594.0790	2.7738
45	0.4512 ± 0.0004	0.4515 ± 0.0003	0.0003 ± 0.0004	1327.9412	3.1232
50	0.4514 ± 0.0006	0.4515 ± 0.0003	0.0001 ± 0.0006	3010.0000	3.4786
60	0.4515 ± 0.0003	0.4515 ± 0.0003	0	-	-

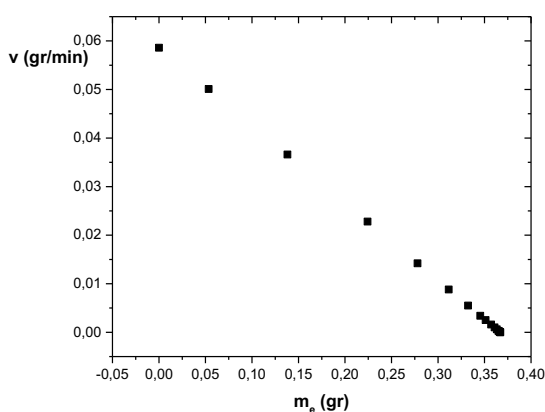


Fig. 6: Massic velocity (v) versus extracted mass of oleoresin with its content (m_e) at 250 rpm.

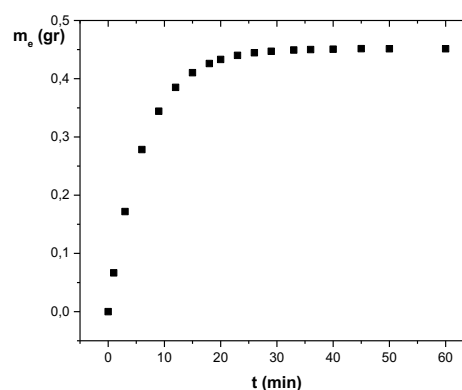
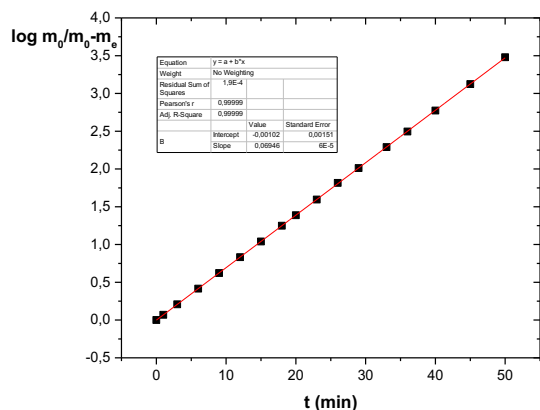
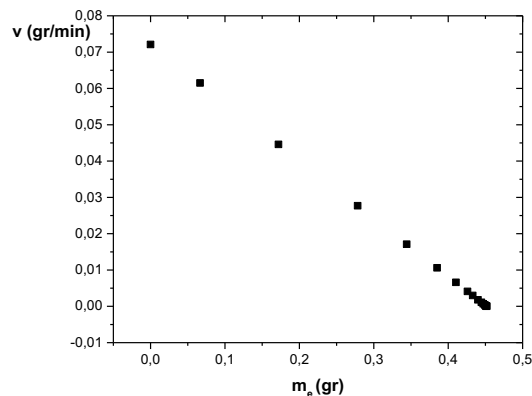


Fig.7: Extracted mass (m_e) of oleoresin containing curcuminoids versus stirring time at 500 rpm.

Fig. 8: $\log\left(\frac{m_0}{m_0-m_e}\right)$ versus stirring time at 500 rpmFig. 9: Massic velocity (v) versus the extracted mass of oleoresin with its content (m_e) at 500 rpm.TABLE IV. MASSIC VELOCITY (v) AS A FUNCTION OF EXTRACTED MASS OF OLEORESIN CONTAINING CURCUMINOIDS (m_e) AT 500 RMP

Temps (min)	m_e (gr)	m_0 (gr)	$m_0 - m_e$	k (min ⁻¹)	v (gr/min)
0	0	0.4515 \pm 0.0003	0.4515 \pm 0.0003	0.1597 \pm 0.0012	0.0721 \pm 0.0000
1	0.0666 \pm 0.0004	0.4515 \pm 0.0003	0.3849 \pm 0.0004	0.1597 \pm 0.0012	0.0615 \pm 0.00006
3	0.1619 \pm 0.0005	0.4515 \pm 0.0003	0.2896 \pm 0.0005	0.1597 \pm 0.0012	0.0446 \pm 0.00008
6	0.2783 \pm 0.0003	0.4515 \pm 0.0003	0.1732 \pm 0.0003	0.1597 \pm 0.0012	0.0277 \pm 0.00005
9	0.3442 \pm 0.0006	0.4515 \pm 0.0003	0.1073 \pm 0.0006	0.1597 \pm 0.0012	0.0171 \pm 0.00010
12	0.3851 \pm 0.0003	0.4515 \pm 0.0003	0.0664 \pm 0.0003	0.1597 \pm 0.0012	0.0106 \pm 0.00005
15	0.4104 \pm 0.0004	0.4515 \pm 0.0003	0.0414 \pm 0.0004	0.1597 \pm 0.0012	0.0066 \pm 0.00006
18	0.4260 \pm 0.0004	0.4515 \pm 0.0003	0.0255 \pm 0.0004	0.1597 \pm 0.0012	0.0041 \pm 0.00006
20	0.4330 \pm 0.0006	0.4515 \pm 0.0003	0.0185 \pm 0.0006	0.1597 \pm 0.0012	0.0030 \pm 0.00010
23	0.4400 \pm 0.0005	0.4515 \pm 0.0003	0.0115 \pm 0.0005	0.1597 \pm 0.0012	0.0018 \pm 0.00008
26	0.4446 \pm 0.0004	0.4515 \pm 0.0003	0.0069 \pm 0.0004	0.1597 \pm 0.0012	0.0011 \pm 0.00006
29	0.4471 \pm 0.0005	0.4515 \pm 0.0003	0.0044 \pm 0.0005	0.1597 \pm 0.0012	0.0007 \pm 0.00008
33	0.4492 \pm 0.0006	0.4515 \pm 0.0003	0.0023 \pm 0.0006	0.1597 \pm 0.0012	0.0004 \pm 0.00010
36	0.4501 \pm 0.0003	0.4515 \pm 0.0003	0.0014 \pm 0.0003	0.1597 \pm 0.0012	0.0002 \pm 0.00005
40	0.4507 \pm 0.0005	0.4515 \pm 0.0003	0.0008 \pm 0.0005	0.1597 \pm 0.0012	0.0001 \pm 0.00005
45	0.4512 \pm 0.0004	0.4515 \pm 0.0003	0.0003 \pm 0.0004	0.1597 \pm 0.0012	0.00005 \pm 0.00006
50	0.4514 \pm 0.0006	0.4515 \pm 0.0003	0.0001 \pm 0.0006	0.1597 \pm 0.0012	0.00003 \pm 0.00010
60	0.4515 \pm 0.0003	0.4515 \pm 0.0003	0	0.1597 \pm 0.0012	0

In Table IV, it can be observed the evolution of massic velocity (v) with the increase of extracted mass of oleoresin with its content (m_e) in ethanol. The decrease of massic velocity has been also evidenced without surprise at 27.5 °C in accordance with (18), suggesting the ethanol saturation in curcuminoids for a given sample as it is shown in Fig. 9.

It should be noted here that Fig. 6 and Fig. 9 have of course the same slope. What is the physical meaning of the value of massic velocity appearing in the last column at time zero as well at 250 rpm as at 500 rpm while the extracted mass (m_e) of oleoresin containing curcuminoids is zero, the extraction has not yet begun? This value which arises from the definition of massic velocity (18) can be explained as a potential massic velocity obtained by extrapolation, not yet in action. It will be in action when the extraction begins with the contact of ethanol with turmeric powder. So it has been decided to write this value with an asterisk in both Table II and Table IV.

This value of the global kinetic constant of oleoresin-containing curcuminoids together with the conversion rate γ can be used to size a closed continuous stirrer pilot tank (reactor) means to determine the reactor volume if the desired volumic debit (Q) is known using the sizing factor (41). Note that the global kinetic constant (k) and the conversion rate ($\gamma = 37\%$) are determined here at the same temperature (27.5 °C) and in the same environment.

Let us take for example γ calculated by $\frac{m}{M}$ (where m is the extracted total mass of oleoresin containing curcuminoids in ethanol and M is the mass of the sample) supposed to correspond exactly with Equation (60).

$$\gamma = \frac{C_0 - C}{C_0} = 1 - \frac{C}{C_0} = 1 - \frac{1}{1 + k\theta} = \frac{k\theta}{1 + k\theta} \quad (60)$$

Equation (61) can be used as it is shown in Table V and Fig. 10.

$$V_r = AQ \quad (61)$$

There is a linear relation between reactor volume and desired debit in both situations (250 rpm and 500 rpm). The calculations of extraction enthalpy and extraction entropy are hereby discussed. The values of ΔH and ΔS have been also calculated.

TABLE V: REACTOR VOLUME AS A FUNCTION OF DESIRED VOLUMIC DEBIT (250 RPM)

Q (l/min)	V (l)
0	0.0000
1	3.6291
1.5	5.4436
2	7.2582
2.5	9.0728
3	10.8873
3.5	12.7018
4	14.5164
4.5	16.3310
5	18.1455

TABLE VI: REACTOR VOLUME AS A FUNCTION OF VOLUMIC DEBIT (500 RPM)

Q (l/min)	V (l)
0	0.0000
1	5.1541
1.5	7.7312
2	10.3082
2.5	12.8852
3	15.4623
3.5	18.0394
4	20.6164
4.5	23.1934
5	25.7705

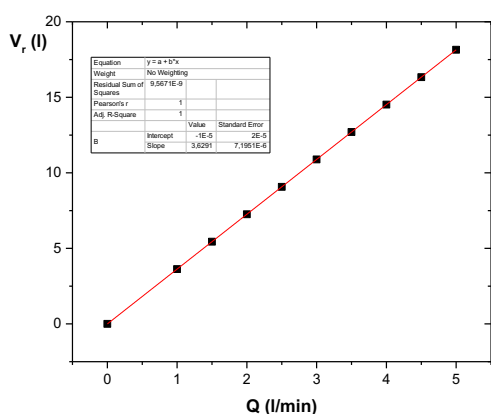


Fig.10: V_r (l) versus Q (l / min) at 250 rpm.

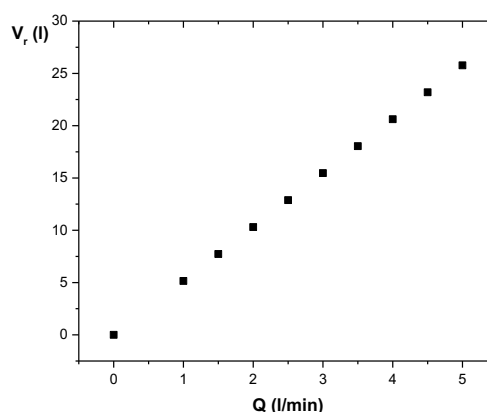


Fig.11: V_r (l) versus Q (l / min) at 500 rpm.

$$\Delta H = -RT \ln k = -8.314 J / molK \times 300.5K \left(\frac{\ln 0.1597}{60 sec} \right) = 76.4 W / mol \quad (62)$$

$$\Delta S = -R \ln k = -8.314 J / molK \left(\frac{\ln 0.1597}{60 sec} \right) = 0.25 W / mol \quad (63)$$

The value of ΔH shows the presence of endothermic phenomenon. This endothermic behavior likely suggests that the solvent with hydroxyl group receives the energy from magnetic stirring and makes possible the solubilization of its alike (like dissolves like), which means in ethanol the enol form of curcuminoids is predominant compared to its tautomeric keto form.

With respect to the positive value of entropy variation, it suggests merely the natural disturbance of the system after the extraction of curcuminoids. The physical meaning of mole in units of ΔH and ΔS is difficult to imagine because the measure has been done on mass of oleoresin containing curcuminoids, material of unknown well defined chemical structure. Nevertheless, this value of ΔH is equivalent to the energy (power) beared per mole to induce extraction or to promote solubilization and its corresponding entropy. The real value of those parameters will be calculated when the compounds of oleoresin will be determined.

CONCLUSION

The establishment of the KUNYIMA first law and the announcement of the KUNYIMA second law bring the scientific revolution in the field of solid-liquid extraction. KUNYIMA's first law and KUNYIMA's second law are elegant tools to undertake the kinetic and thermodynamic study of curcuminoids extraction in closed systems or only kinetic study in an open system. The kinetic constant is a measure of curcuminoids solubility in ethanol. This study has allowed confirming the predominance of the enol form of curcumin in ethanol as a solvent.

The extraction of curcuminoids in ethanol is an endothermic phenomenon and this last phenomenon probably suggests its non-bioavailability.

REFERENCES

- [1] Inano H, Ononda M. Radioprotective action of curcumin longa LINN; inhibitory effect on formation of urinary 8- hydroxy-20- deoxyguanosine, tumorigenesis, but not mortality, induced by gamma-ray irradiation. *International Journal of Radiation Oncology, Biology, Physics*. 2002; 53(3):735-743. DOI: 10.1016/s0360-3016(02)02794-3
- [2] Reddy RC, Vatsala PG, Keshamouni VG, Padmanaban G, Rangarajan PN. Curcumin for malaria therapy. *Biochemical and Biophysical Research Communications*. 2005 Jan 14; 326(2):472-474. DOI: 10.1016/j.bbrc.2004.11.051
- [3] Notarbartolo M, Poma P, Perri D, Dusonchet L, Cervello M, D'Alessandro N. Antitumor effects of curcumin, alone or in combination with cisplatin or doxorubicin, on human hepatic cancer cells. Analysis of their possible relationship to changes in NF-kB activation levels and in IAP gene expression. *Cancer Letters*. 2005 Jun 16; 224(1):53-65. DOI: 10.1016/j.canlet.2004.10.051
- [4] Cui SX, Qu XJ, Xie YY, Zhou L, Naka TM, Makuuchi M, *et al*. Curcumin inhibits telomerase activity in human cancer cell lines. *International Journal of Molecular Medicine*. 2006;18(2): 227-231.
- [5] Hong JH, Ahn KS, Bae E, Jeon SS, Choi HY. The effects of curcumin on the invasiveness of prostate cancer in vitro and in vivo. *Prostate Cancer Prostatic Dis*. 2006; 9:147-52.
- [6] Di Mario F, Cavallaro LG, Nouvenne A, Stefani N, Cavestro GM, Iori V, *et al*. A curcumin-based 1-week triple therapy for eradication of *Helicobacter pylori* infection: something to learn from failure? *Helicobacter*. 2007;12(3):238-243. DOI: 10.1111/j.1523-5378.2007.00497.x
- [7] Johnson JJ, Mukhtar H. Curcumin for chemoprevention of colon cancer. *Cancer Letters*. 2007;255:170-181.
- [8] Kowluru RAA, Kanwar M. Effects of curcumin on retinal oxidative stress and inflammation in diabetes. *Nutr Metab (Lond)* 2007;4:8.
- [9] Li M, Zhang Z, Hill DL, Wang H, Zhang R. Curcumin, a dietary component, has anticancer, chemosensitization, and radiosensitization effects by down-regulating the MDM2 oncogene through the PI3K/mTOR/ETS2 pathway. *Cancer research*. 2007;67(5):1988-1996. DOI: 10.1158/0008-5472.CAN-06-3066
- [10] Sa G, Das T. Anti cancer effects of curcumin: cycle of life and death. *Cell Division*. 2008;3:14. DOI: 10.1186/1747-1028-3-14
- [11] Patel BB, Sengupta R, Qazi S, *et al*. Curcumin enhances the effects of 5-fluorouracil and oxaliplatin in mediating growth inhibition of colon cancer cells by modulating EGFR and IGF-IR. *Int J Cancer*. 2008 Jan 15;122(2):267-73.
- [12] Liju VB, Jeena K, Kuttan R. Chemopreventive Activity of Turmeric Essential Oil and Possible Mechanisms of Action 2014;15:6575-6580.
- [13] Zhou Y, Liu H, Jiang N, Feng X, Zhang H, Wu Z, Liang H, Jiang Q, Chen P. Element, the Essential oil of curcuma wenyujin, Inhibits osteogenic Differentiation in Ankylosing Spondylitis. *Joint Bone Spine*. 2015;82(2):100-103.
- [14] Kunyima AB, Kunyima PM, Kuburhanwa JC, Kunyima MB. Antimyocardial infarctus, efficient Antipoison and Antiprostatae mighty spicy miscellany. *GSJ* 2022;10(4), ISSN 2320-9186. EOI: 10.11216/gsj.2022.04.73584.
- [15] Cherruault Y. Biomathématiques, imprimerie des presses universitaires de France mars 1983 n° 28521.
- [16] Kunyima AB, Kaseya HM, Lusamba SN, Kunyima PK. Matter Transfer in Liquid-Solid Extraction of Democratic Republic of Congo Gourd Seeds Oils by KUNYIMA Method, *Chemical Science Journal*. 2018; 24(4): 1-12. DOI: 10.9734/CSJ/2018/44918.
- [17] Kunyima AB, Kaseya HM, Ntumba MD, Lusamba SN. Democratic Republic of Congo Moringa seeds oil Extraction: KUNYIMA Method Application. *International Research Journal of Pure & Applied Chemistry*. 2019;18(3):1-10. DOI:10.9734/IRJPAC/ 2019/v18i330088.
- [18] Kunyima AB, Kaseya HM, Lusamba SN, Mulaji CK, Ataweza BM. Kunyima Method Validity in Sesame Seeds Oil Extraction, Democratic Republic of Congo. *Chemical Science International Journal*. 2021; 30(1): 11-17. DOI:10.9734/CSJ/2021/v30i130210.
- [19] Kunyima AB, Kaseya HM, Kunyima PL. Experimental Evidence of the Dependence of oil Extraction Rate on Extraction time and structure of Generative Material. *Chemical Science International Journal*. 2021; 30(3): 32-39 N° CSIJ 67899. DOI: 10.9734/CSJI/2021/v30i330222.
- [20] Hombourger C. Le curcuma, de l'épice au médicament. Thèse de Doctorat en pharmacie, Université de LORRAINE (France), 2010.
- [21] Jansen PCM, Grubben GJH, Cardon D. Ressources végétales de l'Afrique tropicale 3. Colorants et tanins. Wageningen, Pays-Bas: PROTA,2005;238