

An investigative study of Diffusion of Commercial Aspirin (Acetylsalicylic acid) in Sodium Hydroxide Solution at 25°C

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Abstract

Diffusion is a macroscopic motion of components of a system that arises from concentration difference. Reaction diffusion is widely used to model developmental process. This project considers effective mechanism leading to effective diffusion coefficient. A mathematical formalism for transforming local transport law into diffusive terms is developed. The diffusion coefficient of drug aspirin was studied in basic NaOH of concentration range 0.01 to 0.1M at 25°C. The rate of diffusion was monitored by observing the boundary conditions of the indicator between the drug and solution. In the study five (5) aspirin tablets collected from a local pharmacy in Eldoret town were used for the study. From the profile it was observed that as the time progressed the boundary increased fast for non-coated tablets compared to the coated ones. All the aspirin were found to give values according to underlying mechanism. For the drug A (600mg) of aspirin the best value of diffusion coefficient of $1.69 \times 10^{-4} \text{ cm}^2 \text{ sec}^{-1}$ was observed while the values for coated drug E with 75 mg aspirin was found to be slightly lower. Fickian mechanism is believed to be the consequence of drug molecule small size. First of all fractional drug uptake is linear and independent of the sample of thickness when $\ln [\text{NaOH}]$ is plotted against square distance. A graph of x^2 against $\ln [\text{NaOH}]$ was plotted which was used to calculate the diffusion coefficient. The experimental values of diffusion coefficient D were within the experimental error to those of $(4Dt)^{-1}$. The study also adopted a descriptive case study; it was conducted at Kimumu municipality, Eldoret town. The target population consisted of 25 respondents. Data was collected using self-administered questionnaires and interview schedules, coded and analysed using SPSS version 16.0. Systematic quantitative review data was analysed using means and frequency tables and percentages while qualitative data was analyzed using inferential statistics chi-square. Data was presented using table, pie charts and graphs. The study found that most of the individuals preferred drug B.

Keywords: Diffusion, Aspirin, Acetylsalicylic acid, Diffusion Coefficient, Sodium Hydroxide, Fickian Mechanism, Systematic Review

INTRODUCTION

Diffusion is a process by which substances are transferred from a region of high concentration to a region of low concentration through random molecular motion. It is a process that involves the existence of proportionality between the rate of flow across any cross section area A and concentration gradient expressed as that cross section. Diffusion as a scientific term has roots in an extremely broad range of disciplines. The concept subsumes the transport of entities as language, populations, genes and technology as well as heat, charge and atoms because of all this process involves a strong element of randomness (Harned and Owen, 1958).

Diffusion in drug systems is described by Fick's second law which in many cases can be analytically solved if experimental data as well as initial and boundary conditions are provided in order to yield an effective mass transfer coefficient. Inversely, when the value of this coefficient is known a mass transfer simulation can be performed and the distribution of concentration in time and space in the drug can be obtained by solving Fick's equation. Analytical solutions covering on varying specimen geometry are found in the most well known (Crank.,1975). The so called effective diffusion coefficient has been used and misused in the drug literature, since drugs are characterised by complicated structure making the media involved and hence forth the mass transfer phenomena multiphase and multi-component.

Consequently the general theory of diffusion must be diffusion process; the entropy is the only increase. In the most elemental spontaneous isothermal mixing, the volume energy and total mole numbers constant. It should not be surprising that the Gaussian and error integral functions from probability play an important role in elemental diffusion theory. Basically solid liquid reactions are more complex than solid gas reactions and include a variety of technically important process such as electro deposition. When a solid reacts with liquid the process involves the products forming a layer on solid surface or dissolving into the liquid phase. If the reaction products are partly or wholly soluble in the liquid phase, the liquid has access to the reacting solid and chemical reaction at the interface therefore becomes important in determining the kinetics (Kays, 2005).

The simplest solid-liquid reaction is the dissolution of a solid in a liquid. The rate of diffusion can be measured by a number of different methods by direct chemical analysis of samples at different distances after definite time intervals. The equations formally describing the diffusing migrations of atoms was proposed over a hundred

years ago (Rinsema, 1999). No experimental data on diffusion was available then and Fick's equations was written in conformity with molecular diffusion within liquids (Jost., 1960). Fick's first law has the following form:

$$J = -D \frac{\partial \phi}{\partial x}$$

Where J (diffusion current is the amount of substance passing through a reference substance of unit time mol/m²·s, x is the co-ordinate perpendicular to surface area where D is the diffusion coefficient length²time⁻¹ (m²/s) and ϕ (for ideal mixtures) is the concentrations in dimensions of (amount of substance) length⁻³, i.e. (mol /m³). The diffusion coefficient controls the rate of diffusion. The dc/dx is the rate change of concentration in the x direction and minus sign indicates the flow from a higher to lower concentrations (Ladler and Meiser, 1982).

In Kenya as a result of trade liberalization and the boost in the local pharmaceutical manufacturing sector, people perceive the pharmaceutical market as a commodity market and an easy means of making profits. The general disregard to lay down rules of quality assurance and desire to reap huge financial profit and the motivating factors for quackery and faking makes it necessary for independent assessment of the quality of pharmaceutical products. Quality assurance is a wide ranging concept covering all matters that individually or collectively influence the quality of a product. Quality assurance incorporates good manufacturing practice (GMP) Quality control as well as other factors including product design and development.

The purpose of quality assurance system is to ensure an absolute quality product such that each product tablet will contain the amount of active drug claimed on the label within the stated limit, as well as other essential parameters such as bioavailability of the product.

MATERIALS AND METHOD

Two concentration sets of base were prepared; dilute and concentrated. To each sample two drops of methyl orange was added and the solution mixed in a disposable plastic cuvettes of cross section 10cm³ and capacity 4.50ml while closed using a fitted stopper. The procedure was repeated with different concentrations of NaOH upto 0.01M. The contents were kept in an oven at a regulated temperature of 25°C.

An accurately weighed mass of commercial aspirin tablets was dropped into each of the cuvettes and time recorded at different intervals where boundary height between the alkaline and acidic parts of solutions formed.

Study Area

The target population comprised of a twenty five personnel based in Kimumu. This is because the sample must be enough to represent the critical characteristics of the target population.

Stratified sampling was used to select respondents to be included in the sample. This technique identifies sub-groups, in the population and their proportions and selected from each sub-groups to form a sample. It groups a population into separate homogeneous that share similar characteristics so as to ensure equitable representation of population in the sample.

Sampling procedure and sample size

Both probability and non-probability sampling procedures were used in selecting samples from the secondary schools. The researcher used cluster or sampling techniques. According to the (Kothari, 2004) cluster sampling technique involving the selection of an interact group rather than individual elements for inclusion than the sample was appropriate for this study. Cluster was the different categories in the area. It is used if the population is scattered over a large geographical area and it is not easy to obtain a sample frame. All members of such intact group in this case the elderly were included in sample and each because a unit of observation.

A small population of 200 or less of the entire population should be used as this enables a researcher to achieve level of precision and sampling error is eliminated as data on all units of observation are provided (Israel, 2008). Data was therefore collected from all schools in the region, (Kombo and Tromp ,2006) recommend the use of table in order to determine size of randomly chose sample for finite populations, thus a population of 25 was represented by the sample. The number of personnel who participated in this study was determined using non probability purposive sampling techniques.

The study employed two instruments for data collection: practical experimental lab work and interview from the questionnaires. They were used to collect data on the efficiency of drug aspirin use for the period 2010 to 2011. The questionnaire had specific questions related to specific objectives and research questions.

An interview schedule (Appendix I) for personnel as in depth data was collected on April 2011. Such information cannot be obtained without using a questionnaire (Mugenda and Mugenda, 1999). The questionnaire is referred to as Appendix I. Both instruments are divided into three parts. Part I seems to establish general information of the personnel. Part II inquires information on the drug aspirin.

Data analysis

Data collected from the field was coded and entered into the computer for analysis using the statistical package for social science (SPSS version 18.0). Descriptive statistics including percentage and frequency count were used to analyze the data obtained (Bell and Rhodes 1996) maintains that when making the results known to a variety of readers, simple descriptive statistics such as percentages have a considerable advantage over complex statistics since they are easily understood (Olemba and Ross ,1992) also hold that the most widely used and understood standard proportion is the percentage. The results of data analysis both from laboratory and field were presented in frequency tables and bar graphs.

Results

The more soluble a drug is, the more quickly it passes from the digestive system into the bloodstream after being swallowed. Aspirin is a weak acid and methyl orange indicator was found to be a suitable indicator. The concentration of a simple case of solution containing a single solute. The solute spontaneously diffuses from a region of high concentration to one of low concentration. Chemically speaking the driving force of diffusion is the gradient of potential, but it is more usual to think of the diffusion of solutes in terms of gradient of their concentration. Although no individual solute particle in a particular volume shows a preference for motion in a particular direction, a definite fraction of molecules may be considered to be moving in any particular direction, for instance the x direction. In an adjacent volume the same volume may be moving in reverse direction. If the concentration in the first volume is greater than in the second, the overall effect is that more particles moving are leaving the first element for second and hence a net flow of solute in the x direction, the direction of decreasing concentration. This was governed by Fick's law.

Experiment with Sodium Hydroxide solution from 0.01M TO 0.10M

The research showed typical data from a run using sodium hydroxide after an initial period of about one hour the rate of rising of the hydroxide was proportional to time and was dependent on the concentration of the bases and the weight of the commercial aspirin tablet. When the square of the height of the boundaries were plotted against time, straight lines passing near the origin were obtained (figure 2) the slopes of these plots were found to be dependent on the basic concentrations.

The rates of diffusion of aspirin in sodium hydroxide solutions increased with increased concentration of the base: - a solution that, agreed with expectations of diffusions with chemical reactions.

Experiments with Sodium Hydroxide solution from 0.10M TO 1.0M

The research showed the results of the basic solutions with concentration between 0.1M and 1.0M. The results may be classified into three groups.

1. 0.10-0.40M: acid has quantities of aspirin that are higher than those of the base into the solutions therefore the aspirin diffuses to the meniscus.
2. 0.50M base is in a class of its own: this type of behavior is observed when the number of moles of moles of aspirin is equal (or almost equal) to those of moles of OH⁻ in the basic solutions of the steady state at which the boundary remains at the same positions for a long time interval indicates a situation where the rate of diffusion of the aspirin is exactly counter balanced by the rate of diffusion of the base.
3. 0.6M - 1.0M base: the amounts of base in such solutions usually exceed the quantity of acid in the tablet. Hence initially the acid diffuses into the base to a height that depends on the concentration of the base, after which the tablet begins to diffuse into the alkali.

When the squares of the boundaries were plotted against time, straight lines passing near the origin were obtained.

As the concentrations increased, the plots could not yield straight lines as the boundaries started dropping due to the fact that the base begins to diffuse into the acid.

The results also agree with the square root relationship for the diffusions into a semi-infinite medium involving the dimensionless parameter (Crank., 1975):

In two aspects;

1. The distance obtained by any given concentration was proportional to the square root of the time.
2. The time needed for any point to reach a given concentration is proportional to the square of its distance from the surface where the diffusion occurs.

Table 1: Data of basic concentrations and diffusion coefficient for Drug A (0.01M to 0.1M).

Mass (grams)	Concentration	Slope $V \times 10^{-4}$	$D \times 10^{-6}$	Square roots	$D' \times \text{square root}$ $D' \times 10^{-6}$
1.120	0.01	9.42×10^{-4}	7.5×10^{-4}	$\sqrt{0.01}$	7.50
1.121	0.02	6.50×10^{-4}	5.17×10^{-5}	$\sqrt{0.02}$	7.31
1.120	0.03	5.46×10^{-4}	4.36×10^{-5}	$\sqrt{0.03}$	7.55
1.122	0.04	4.90×10^{-4}	3.91×10^{-5}	$\sqrt{0.04}$	7.82
1.120	0.05	4.39×10^{-4}	3.52×10^{-5}	$\sqrt{0.05}$	7.88
1.121	0.06	3.54×10^{-4}	2.84×10^{-5}	$\sqrt{0.06}$	6.98
1.121	0.07	3.05×10^{-4}	2.42×10^{-5}	$\sqrt{0.07}$	6.42
1.120	0.08	2.80×10^{-4}	2.23×10^{-5}	$\sqrt{0.08}$	6.30
1.122	0.09	2.57×10^{-4}	2.05×10^{-5}	$\sqrt{0.09}$	6.14
1.122	0.10	2.40×10^{-4}	1.91×10^{-5}	$\sqrt{0.10}$	6.05

$69.95 \times 10^{-6} \text{ cm}^2 \text{ sec}^{-1}$

Table 2: Data of basic concentrations and diffusion Coefficient for Drug A (0.1 to 1M)

Mass (grams)	Concentration	Slope $V \times 10^{-5}$	$D \times 10^{-6}$	Square roots	$D' \times \text{square root}$ $D' \times 10^{-6}$
1.120	0.1	7.19	5.72	$\sqrt{0.1}$	1.81
1.121	0.2	5.91	4.69	$\sqrt{0.2}$	2.10
1.120	0.3	5.53	4.40	$\sqrt{0.3}$	2.41
1.122	0.4	5.18	4.14	$\sqrt{0.4}$	2.62
1.120	0.5	4.87	3.87	$\sqrt{0.5}$	2.72
1.121	0.6	4.68	3.74	$\sqrt{0.6}$	2.90
1.121	0.7	4.46	3.56	$\sqrt{0.7}$	2.98
1.120	0.8	4.58	3.64	$\sqrt{0.8}$	3.26
1.122	0.9	4.62	3.67	$\sqrt{0.9}$	3.48
1.122	1.0	4.40	3.52	$\sqrt{1.0}$	3.52

Total value $27.80 \times 10^{-6} \text{ cm}^2 \text{ sec}^{-1}$

The average diffusion coefficient value is $4.89 \times 10^{-5} \text{ cm}^2 \text{ sec}^{-1}$

Table 3: Data of basic concentrations and diffusion coefficient for Drug E (0.01 to 0.1M)

Mass (grams)	Concentration	Slope $V \times 10^{-9}$	D	Square roots	$D' \times \text{square root}$ $D' \times 10^{-10}$
0.120	0.01	1.38×10^{-8}	1.1×10^{-9}	$\sqrt{0.01}$	1.1
0.121	0.02	1.00×10^{-8}	7.8×10^{-10}	$\sqrt{0.02}$	1.13
0.120	0.03	8.67×10^{-9}	6.9×10^{-10}	$\sqrt{0.03}$	1.19
0.121	0.04	7.79×10^{-9}	6.2×10^{-10}	$\sqrt{0.04}$	1.24
0.120	0.05	7.35×10^{-9}	5.85×10^{-10}	$\sqrt{0.05}$	1.31
0.121	0.06	7.07×10^{-9}	5.63×10^{-10}	$\sqrt{0.06}$	1.38
0.121	0.07	7.07×10^{-9}	5.63×10^{-10}	$\sqrt{0.07}$	1.49
0.120	0.08	6.98×10^{-9}	5.55×10^{-10}	$\sqrt{0.08}$	1.57
0.120	0.09	6.97×10^{-9}	5.55×10^{-10}	$\sqrt{0.09}$	1.64
0.121	0.10	6.87×10^{-9}	5.50×10^{-10}	$\sqrt{0.10}$	1.73

$13.78 \times 10^{-10} \text{ cm}^2 \text{ sec}^{-1}$

Table 4: Data of basic concentrations and diffusion coefficient for drug E (0.1M TO 1M).

Mass (grams)	Concentration	Slope $V \times 10^{-9}$	$D \times 10^{-10}$	Square roots	$D' \times \text{square root}$ $D' \times 10^{-10}$
0.120	0.1	1.16×10^{-8}	9.23×10^{-10}	$\sqrt{0.1}$	2.92
0.121	0.2	8.04×10^{-9}	6.40	$\sqrt{0.2}$	2.86
0.120	0.3	6.11×10^{-9}	4.87	$\sqrt{0.3}$	2.67
0.121	0.4	4.81×10^{-9}	3.83	$\sqrt{0.4}$	2.42
0.120	0.5	3.93×10^{-9}	3.13	$\sqrt{0.5}$	2.21
0.121	0.6	3.46×10^{-9}	2.75	$\sqrt{0.6}$	2.13
0.121	0.7	3.01×10^{-9}	2.40	$\sqrt{0.7}$	2.01
0.120	0.8	2.78×10^{-9}	2.21	$\sqrt{0.8}$	1.98
0.120	0.9	1.72×10^{-9}	1.37	$\sqrt{0.9}$	1.30
0.121	1.0	1.53×10^{-9}	1.22	$\sqrt{1.0}$	1.22

$21.72 \times 10^{-10} \text{ cm}^2 \text{ sec}^{-1}$

The average diffusion coefficient value is $1.78 \times 10^{-9} \text{ cm}^2 \text{ sec}^{-1}$

The plots of height squared against time for the drug of concentration ranging from 0.01 to 0.1 for the aspirin drug A and E are shown from figure 2 while those of $\ln [\text{NaOH}]$ against x^2 are illustrated as from figure 1

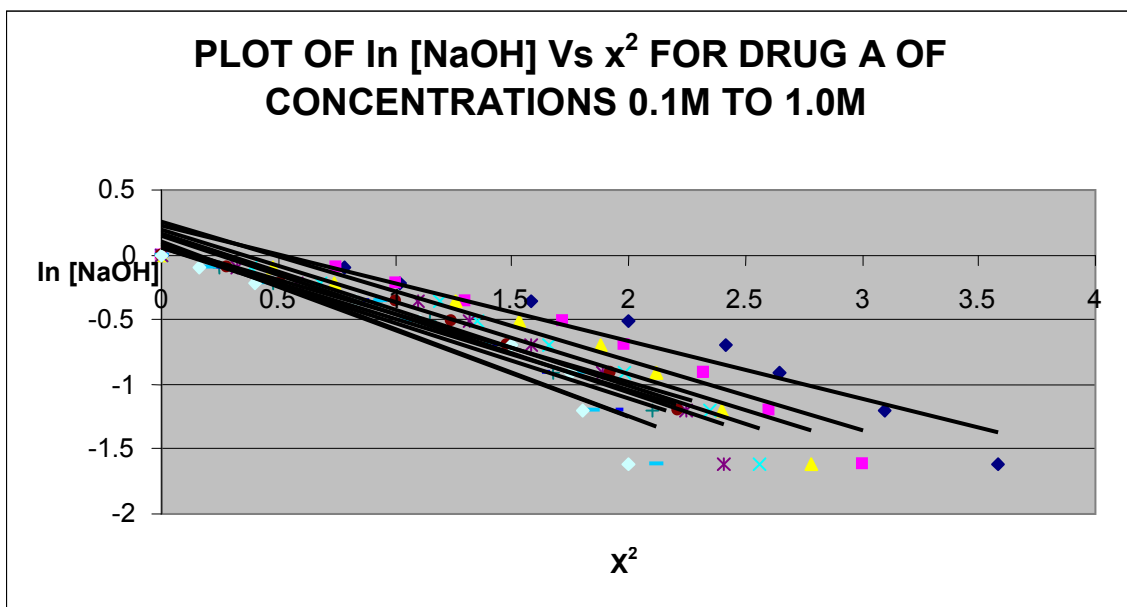


Figure 1: Graph of $\ln [\text{NaOH}]$ versus x^2 for drug A (0.1M TO 1.0M).

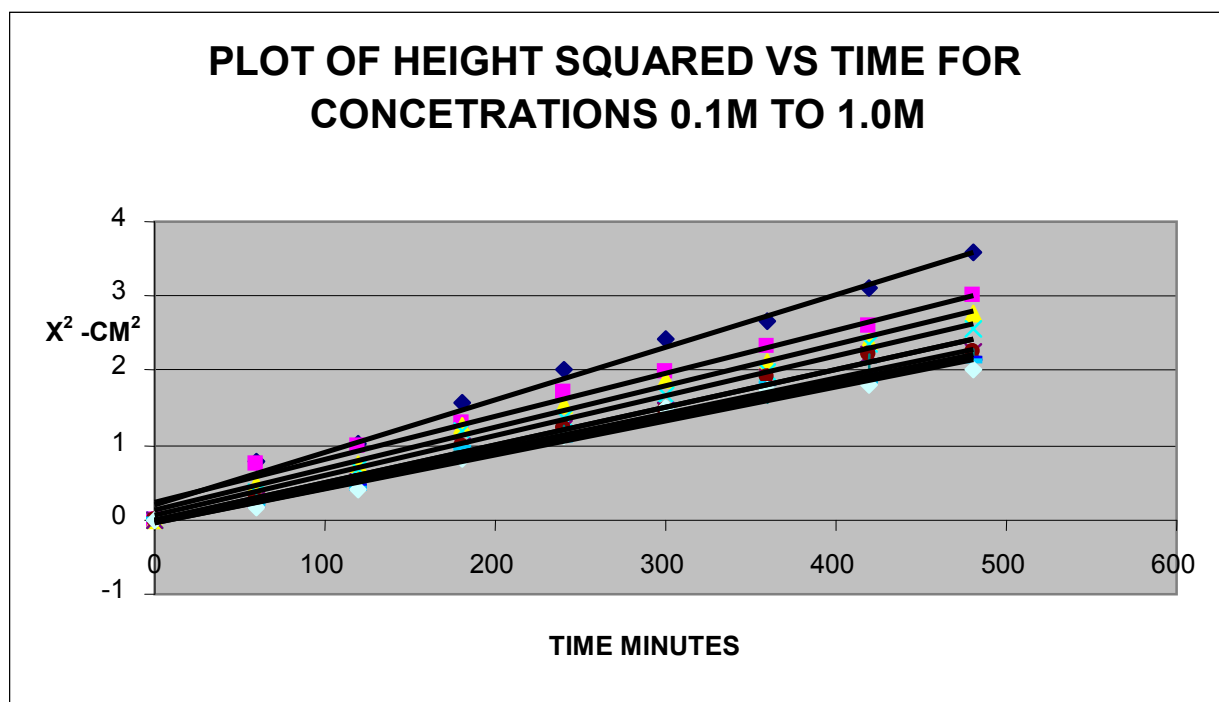


Figure 2: Graph of x^2 versus time for 0.1M to 1.0M sodium hydroxide solutions for DRUG A 0.1M TO 1.0M

Comparison methods of diffusion coefficient for commercial aspirin

The diffusion coefficient for a strong electrolyte at infinite dilution may be calculated from the equation (27),

$$D_0 = \frac{8.936 \times 10^{-10} T (v_1 + v_2) h_1^0 h_2^0}{v_1 z_1 (h_1^0 + h_2^0)} \dots \dots \dots (27)$$

Where T is the absolute temperature, v_1, v_2 are the numbers of cations and anions from dissolution of one molecule of the electrolyte, z, cationic charge Λ^+ and Λ^- equivalent cation and anion limiting conductances.

$$D_0 = \frac{8.936 \times 10^{-10} T \times 2(50 \times 10^{-04} \times 36 \times 10^{-04})}{(50 \times 10^{-04} + 36 \times 10^{-04})} = 1.11 \times 10^{-9} \text{ cm}^2 \text{sec}^{-1}$$

$$\Lambda^0 = \nu_+ \Lambda_+ + \nu_- \Lambda_-$$

$$1 \times 50.08 \times 10^{-4} + 1 \times 36 \times 10^{-4}$$

$$= 86.08 \times 10^{-4}$$

$$D = \frac{RT\Lambda}{z^2 F^2}$$

$$D = \frac{8.936 \times 10^{-10} T \times 2(86 \times 10^{-04})}{2(96000)^2}$$

$$= 1.15 \times 10^{-9} \text{ cm}^2 \text{sec}^{-1}$$

$$D = \frac{2DA \times DB}{DA + DB}$$

$$D = \frac{2 \times 9.58 \times 10^{-10} \times 1.33 \times 10^{-5}}{9.58 \times 10^{-10} + 1.33 \times 10^{-5}}$$

$$= 1.92 \times 10^{-9} \text{ cm}^2 \text{sec}^{-1}$$

The D values for sodium and salicylate are 1.33×10^{-5} and $9.58 \times 10^{-10} \text{ cm}^2 \text{sec}^{-1}$ respectively while the limiting conductances are 50.08×10^{-4} and $36 \times 10^{-4} \text{ m}^2 \text{Smol}^{-1}$. The values obtained are close from the one from the moving boundary method. The effect of electrostatic interaction of electroneutrality is the retardation of diffusion of salicylate ions and the acceleration of the diffusion of Na^+ .

Questionnaire Return Rate

Twenty five (25) individuals were selected and issued with questionnaire seeking to establish their perceptions on the efficiency of the drug aspirin. Out of the 25 issued with interview schedules of them returned dully filled lists making an interview schedule return rate of 93.3%, 68% returned dull filled in questionnaires which represents 88.3% return rate. The overall return rate was 90.8% which the researcher found to be adequate representative of the target population. There is no standard for an acceptable response rate (Merrill, 2002), but published opinion indicates that below 80% bias is likely to occur and a response rate above 60% is acceptable. The age group of the individuals using drug aspirin is presented in table 5.

Table 5: Age group of the individuals using drug aspirin

Age group of the Individuals using Drug Aspirin	Frequency	Percent
Adults	17	68.0
Both of them	5	20.0
Children	3	12.0
Total	25	100.0

Reasons for using drug aspirin

The analysis found the reason for using drug aspirin were numerous, 28% said on health benefits, 12% said awareness. Therefore the best reason for using the drug aspirin was health benefits. Table 6 shows the reasons for using drug aspirin.

Table 6: Reasons for using aspirin drug

Reasons for using drug aspirin	Frequency	Percent
Awareness	3	12.0
Health benefits	7	28.0
Access to drug product	4	16.0
Government policy	6	24.0
Availability of drug product	5	20.0
Total	25	100.0

CONCLUSION

The use of the diffusivity data may be used cautiously by the chemists, taking into account the special issues associated with the concept of this drug property.

Based on the findings of the study of number of conclusion were drawn.

All the aspirin tablet were found to produce values according to underlying mechanism. For the drug A loaded with 600mg of aspirin the best value of diffusion coefficient of $4.89 \times 10^{-5} \text{ cm}^2 \text{ sec}^{-1}$ was observed while the values for coated drug E with 75mg aspirin was found to be slightly lower ($2.49 \times 10^{-9} \text{ cm}^2 \text{ sec}^{-1}$).

Although the experimental technique described is a simple and needs no intricate equipment, it yields D values that are close to those calculated and from limiting conditions within experimental error.

The absence of an opposing applied force, all solutes tend to diffuse through solutions until the compositions are homogeneous throughout. Small molecules move with sufficient velocity to distribute the molecule throughout the solvent rapidly.

The rates at which a substance diffuses across a unit cross-sectional area depend not only on the molecular size and shape but also on the concentration gradient of the substance.

The diffusion coefficient can be recognised as the amount of solute that diffuses across a unit area in one sec under the influence of a unit concentration gradient. It was realised that the function had temperature dependence.

A graph of x^2 against $\ln [\text{NaOH}]$ was plotted which was used to calculate the diffusion coefficient. The experimental values of diffusion coefficient D were within the experimental error to those of $(4Dt)^{-1}$. The test with ANOVA produced a result of no significant difference among the five drugs. Aspirin which hydrolyses into salicylic acid and should therefore be protected by monitoring and controlling the moisture content during production.

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