

DETERMINATION OF QUALITY DETERIORATION INDEX OF SOME COMMONLY USED DRUGS, USING ELECTRICAL CONDUCTIVITY, CHARGE DENSITY AND pH VALUESUshie, P.O¹; Kamgba, F.A¹; Osahon, O.D²; Edet, C.O¹¹Department of Physics, Cross River University of Technology, Calabar, Nigeria.²Department of Physics, Faculty of Physical Sciences, University of Benin, Benin City, Nigeria.***Corresponding Author: Dr. Ushie P. O.**

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ABSTRACT

Aim: This study was factored out with the aim of determining the quality deterioration of some commonly used drugs (Vitamin C, Paracetamol, Panadol, Aspirin and Flagyl), using well known parameters like electrical conductivity, charge density and pH. **Objectives:** The use of medicine is often complex, the supply cycle needs to be well managed to prevent all types of wastage, including abuse and use of expired ones. This wastage reduces the quantity of medicines available to patients and therefore the quality of health care they receive. **Materials and Method:** The data obtained from the parameters (electrical conductivity, charge density and pH) were analysed and an equation developed using well known relations to establish a relationship between charge density, electrical conductivity, mass, time and charge. **Result and Data Analysis:** For the unexpired drugs (same drugs sample); a maximum and minimum value of $(35.66 \pm 0.35$ and $17.29 \pm 0.24)$ $\mu\text{S}/\text{cm}$ for conductivity, pH of $(6.55 \pm 0.17$ and $7.80 \pm 0.26)$ measured at a concentration of $0.5\text{g}/100\text{cm}^3$ and a maximum and minimum value of $(3.202\text{E}-22$ and $6.604\text{E}-22)$ C/m^3 for Charge density. While the expired drugs samples, has maximum and minimum values of $(13.38 \pm 0.22$ and $22.15 \pm 0.17)$ $\mu\text{S}/\text{cm}$, pH of $(5.58 \pm 0.24$ and $11.15 \pm 0.17)$ measured at the same concentration and a maximum and minimum value of $(2.509\text{E}-22$ and $4.153\text{E}-22)$ C/m^3 for Charge Density. **Discussion and Conclusion:** The relatively high conductivity value of the unexpired drugs shows the high number of ions available in the conduction process of absorption by the body fluid. While the relatively low conductivity values from the expired drugs shows that it will take longer time to be absorbed by the body cells. This is perfectly in agreement with the charge density obtained from the physical equation developed.

KEYWORD: Drugs, charge density, electrical conductivity, deterioration index, pH.**1. INTRODUCTION**

Any substance taken orally or by infusion and has the potentials to prevent and treat diseases or to enhance physical and mental well-being can be regarded as a drug [Stedman, 2014]. Drugs can be naturally occurring or synthetic. A soft drug is less addictive and considered less harmful to the body and to society as a whole, while hard drugs are harshly addictive and considered much more harmful to the body and society in general. These are the two ways in which drugs are being classified [Cooltony 2009]. Currently, some commonly used drugs are available to determine their quality deterioration using physical parameters. These drugs are expired and unexpired. The ionic response of a drug to the body medium is a measure of the electrical conductivity of such a drug. Electrical conductivity is defined as the ratio between the current density (J) and the electric field density (E) and it's the inverse of resistivity. An electric current result from the motion of electrically charged

particles in response to forces that act on them from an applied electric field (Lanntech BV) within most solid materials a current arises from the flow of electrons, which is called electronic conduction. In all conductors, semiconductors and many insulated materials only electronic conduction exist and the electrical conductivity is strongly dependent on the number of electrons available to participate to the conduction process. Most metals are extremely good conductors of electricity because of the charge number of free electrons that can be excited in an empty and available energy state. In water and tonic materials or fluids a net motion of charged ions can occur. This phenomenon produces an electric current and is called ionic conductor [Maes, 1981]. Quality drugs is important and is one of the earliest to come under government security, to a greater extent determine some commonly used drugs that deteriorate when expired. It is important to have some

basic knowledge of the International Conference on Harmonisation (ICT).

1.1 Development and Manufacturing of Drugs: The goal of manufacturing process and development for the drug substance is to establish a commercial manufacturing process capable of consistently producing drug substance of the intended quality. These processes should be determined through consideration of its use in the drug product as well as from knowledge and understanding of its physical, chemical, biological and micro-biological properties or characteristics, which can influence the development of drugs product (e.g the solubility of the drugs substance can affect the choice of the dosage form).

One of the requirement needed for the manufacturer of quality drug substances are validated processes capable of providing repeatable results. In support of accomplishing the task of manufacturing quality product, manufacturing process development requires adherence with six quality principles delineated viz-a-viz

- 1) Drug substances quality linked to drug product
- 2) Process development tools
- 3) Drugs substance
- 4) Linking material attributes and process parameters to drugs substance
- 5) Design space

Contributing factors to expired and unexpired drugs in supply facilities were common among medicines for vertical health programmes, with percentage of outlet reporting expired and unexpired drugs including, vitamin C, Paracetamol, Panadol, Aspirin, Flagyl tablets etc.

1.2 Purposes of Drugs Testing: Over the past decades, drug testing has been used worldwide in a variety of disciplines including criminal justice, emergency medicine, clinical toxicology and work place. Drug testing plays an important role in facilitating the judicial sentence of drug abusers in courts, drug surveillance programme of inmates who are detained under the custody of drug treatment centres, as well as the enforcement of the legislation of driving under the influence by the police. Timely and reliable drug test result is of prime importance in the field of emergency medicine and clinical toxicology. The objective of testing is focused on determining the class of drugs that has been inadvertently or purposely ingested or exposed to the patterns. Mortalities and morbidities would then be greatly reduced by effective, appropriate and prompt antidote treatment or supportive care [Tam –Wai, 2008].

1.3 Submission of Relevant Information: In support of the submission process, manufacturers are required to provide a list of the raw materials being used and their specifications supported by written justification as to why these materials are acceptable. This Justification is required for synthetic, semi-synthetic, and biotechnological/biological drug substance.

1.4 General Drug Quality Tests: There are many indicators of drugs quality as described in literature. Some of these can be performed at facilities with modest infrastructure while others require more substantial investment.

They can broadly be classified as

- 1) Physical test that include visual inspection.
- 2) Chemical tests for content of active ingredients and impurities under normal and stimulated storage condition.
- 3) In vitro disintegration and dissolution tests and.
- 4) In vivo bioavailability studies.

Thus, physical test may include tests done on liquid, semi-solid and solid pharmaceutical dosage forms. For instance, for tablets uniformity of weight, friability (how well a tablet holds under normal conditions of transportation, measured by the proportion of the tablet that is lost as powder), tablet hardness, and so on, can test be carried out as part of the quality test.

For instance, the test for content determines the amount of active ingredient in a product, which is expressed as a percentage of the label claim, while the dissolution test determines that amount of active ingredient that is released from the dosage form and available for absorption, and is used as surrogate marker of in vivo bioavailability for oral dosage forms containing poorly aqueous soluble drugs such as sulfadiazine-pyrimidine. Other tests for quality which have been reported in the literature review are briefly described below.

1.5 Stability Tests and Product Shelf Life: Stability tests are performed as part of the quality assessment of a drugs product when stored under specified conditions of temperature and moisture. They assess the ability of a drug product to remain stable with reference to identity, strength and purity throughout its stated shelf life. Stability studies are designed to test the integrity of the active ingredients under a range of conditions that mimic what would be expected during transportation, storage, handling and usage. Specifications for testing the stability of drugs have been standardised over the years for the purpose of regulatory approval under the control of the International Conference on Harmonisation (ICH). There are currently three categories of stability studies: long term, Intermediate and accelerated stability studies. Under current ICH guidelines, long term and intermediate stability studies are carried out under the temperature of intended storage of the drug product and the active ingredients and duration product quantified every 3 months, studies should cover a minimum of 12 and 6 months respectively and the data is submitted to regulatory authorities, together with a schedule of when other submissions will be made, post registration for the labelled shelf life of the drug. However, more common is the accelerated stability studies where the drug products are subjected to elevated temperatures and humidity for 6 months. Data from the 6 months period

are extrapolated using computer programmes that take into consideration the intended range of storage conditions for the given product. A minimum of three batches are analysed and the data pooled to give estimated product shelf life. Statistical test of heterogeneity is used to determine if the result from the test batches can be pooled or if more tests need to be done to give a better estimate of shelf life.

Charge density of drug is another method propounded as a measure to test the viability, potency and quality of drug by using simple mathematical formulations.

1.6 The Global Problem of Drug Quality: About 15% of all drugs in circulation worldwide are believed to be counterfeits, with the figures rising to as high as 50% in some parts of Africa and Asia [Schultz, 1961]. Counterfeit ranitidine (anti-ulcer drug) and tadalafil (anti-impotent drug) have been reported in the United Kingdom in 1994 and 2004 respectively; but in Nigeria some commonly used drugs are reported as abused by the society (codine and tramadol as hard drugs). For diseases like malaria where progression from mild to severe disease is rapid, especially in young children giving drugs with little or no active ingredient has been said to be "tantamount to murder" giving drugs with no active ingredient or with the wrong active ingredients means the patient will not be cured of malaria and there is a good chance such a patient will die. Giving patient anti malaria drugs with sub-therapeutic levels of the drug means drug-resistant parasites will be selected in given population. This, in turn, means a switch to using newer and more expensive drugs. A balance has to be struck between the need to make affordable anti malaria drugs available where the majority of the people live, and ensuring that in the process the quality of the drugs is not compromised.

2. Mathematical Formulation

Some mathematical relations were evaluated as follows to determine the charge density from measured parameters;

$$j = \frac{I}{A} \quad (1)$$

and

$$j = \sigma E \quad (2)$$

Where j = current density, I = current, A = surface area, E = electric field, and σ = conductivity

Equating Eqs. (1) and (2) we have

$$\frac{I}{A} = \sigma E \quad (3)$$

$$\text{But } I = \frac{q}{t} \quad (4)$$

Substitute EQ. (4) into (3) and multiply both side by $\frac{1}{l}$ we have

$$\frac{q}{A.l} = \frac{\sigma E t}{l} \quad (5)$$

$$\text{Where } V = A.l \text{ and } \frac{1}{v} = \frac{t}{l}$$

$$\frac{q}{V} = \frac{\sigma E}{v}, \rho = \frac{q}{V} \text{ and } \rho = \frac{\sigma E}{v} \quad (6)$$

$$\mu_{\text{electron mobility}} = \frac{v}{E} \quad (7)$$

Eq. (6) becomes

$$\rho = \frac{\sigma}{\mu} \quad (8)$$

$$F = \frac{mv}{t} \quad (9)$$

$$F = qE \quad (10)$$

Equating Eqs. (9) and (10) we arrived at

$$\frac{mv}{t} = qE \quad (11)$$

Substituting Equation (11) into (6), we have;

$$\rho = \frac{\sigma m}{qt} \quad (12)$$

Where

ρ = Charge density of the substance, σ = conductivity, m = mass of the substance, q = charge of the substance (electronic charge), t = time taken per sample analysis of the substance.

3. MATERIALS AND METHOD

Apparatus/Reagent: Electrostatic oven, mortar and pestle, beakers, measuring cylinder, funnels, pH meter, conductivity meter, glass wool, distilled water, drugs (expired and unexpired), conical flasks and probs.

The drug samples collected for the purpose of this research work are Vitamin C, Paracetamol, Pandol, Aspirin and Flagyl. Expired (collected from pharmacist) and unexpired (bought) commonly used drugs were gotten from pharmaceutical stores situated in Etim Edem Park, Calabar, Cross River State. The conductivity of the sample was measured using digital conductivity meter, model- CS16522 and manufactured by Thermo Scientific united State. Samples of Vitamin C, Pracetamol, Panadol, Aspirin and Flagyl drugs were crushed, weighed and then dissolve in distilled water in a measuring cylinder. The resulting mixture was shaken and allowed to properly dissolve. The conductivity meter probe was immersed in the final solution. With the meter switched on the conductivity value displayed on a liquid crystal (digital read out) was recorded. The experiment was repeated three times using the same solution after which the average value and standard deviation were calculated. This process was carried out for the five samples, with the readings recorded appropriately. The pH of the samples was measured in a similar manner using a pH meter, model- 210A 250A and manufactured by Orion Which generally comprises a detecting unit consisting of a glass electrode and a reference electrode and an indicating unit for indicating the pH value corresponding to the electromotive force detected. The indicating unit usually has dials for zero-point adjustment and temperature compensation. The glass electrodes were immersed previously in distilled water for an hour. Then measurement commenced 10 minutes (600 seconds) after switching on the meter. The detecting units (probes) were properly rinsed with distilled water and allowed to drain thoroughly for some

minutes. After measurements were carried out for a sample, a proper rinsing and draining of the detecting unit was done before commencing with another. The readings for the individual sample were recorded. The experiment was repeated three times using the same solution so that average value and standard deviation can be calculated.

water in a 250 ml beaker with stirring. Filtration was done with glass wool to remove other pellets or particles to a clear solution. The following were adopted for standard procedure;

- Concentration use 0.5 g/100 ml
- 1) Unit of conductivity $\mu\text{S/cm}$
- 2) Temperature 81 °F or 25 °C.

Procedure

0.5 g of each drug were weighed on the analytical electronic balance and dissolved with 100 ml of distilled

4. RESULTS AND DISCUSSION

Table 1: Conductivity and pH of unexpired drugs measured at a concentration of 0.5 g/100 cm³.

Sample code	Drug samples	Conductivity ($\mu\text{S/cm}$)	pH	Charge Density (C/m^3)
A.	Vitamin C	17.29 ± 0.24	6.72 ± 0.24	9.0E13
B.	Aspirin	29.66 ± 0.33	6.55 ± 0.17	15.0E13
C.	Panadol	35.66 ± 0.35	7.65 ± 0.32	18.6E13
D.	Paracetamol	30.24 ± 0.30	7.80 ± 0.26	15.8E1
E.	Flagyl	26.38 ± 0.36	7.43 ± 6.33	13.7E13

Table 2: Conductivity and pH of expired drugs measured at a concentration of 0.5 g/100 cm³.

Sample code	Drug Samples	Conductivity ($\mu\text{S/cm}$)	pH	Charge Density (C/m^3)
A.	Vitamin C	14.50 ± 6.26	6.08 ± 0.24	7.6E13
B.	Aspirin	17.48 ± 0.14	5.58 ± 0.24	9.1E13
C.	Panadol	22.15 ± 0.17	10.20 ± 0.26	11.5E13
D.	Paracetamol	20.73 ± 0.20	11.15 ± 0.17	10.8E1
E.	Flagyl	13.38 ± 0.22	8.42 ± 0.24	7.0E-22

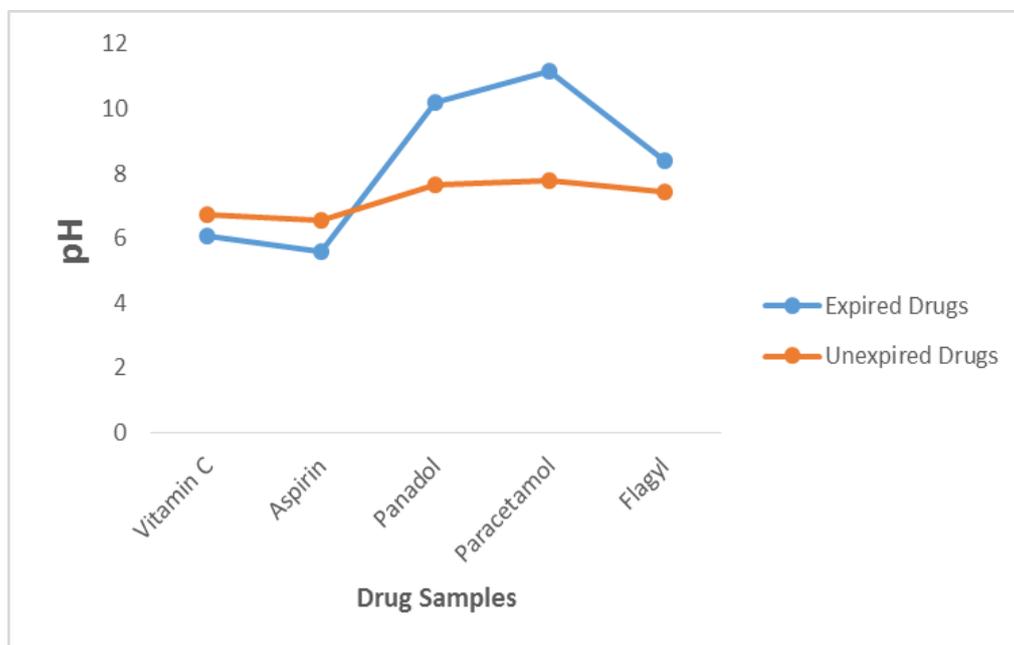


Figure 1; Graph of pH against drug samples.

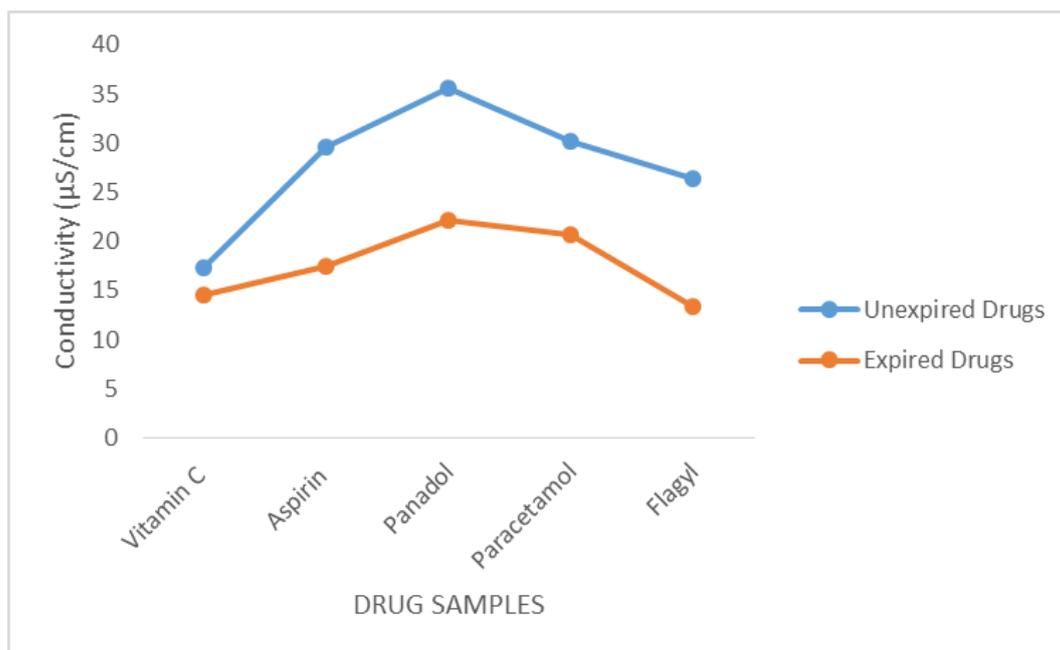


Figure 2: Graph of Conductivity against drugs Samples.

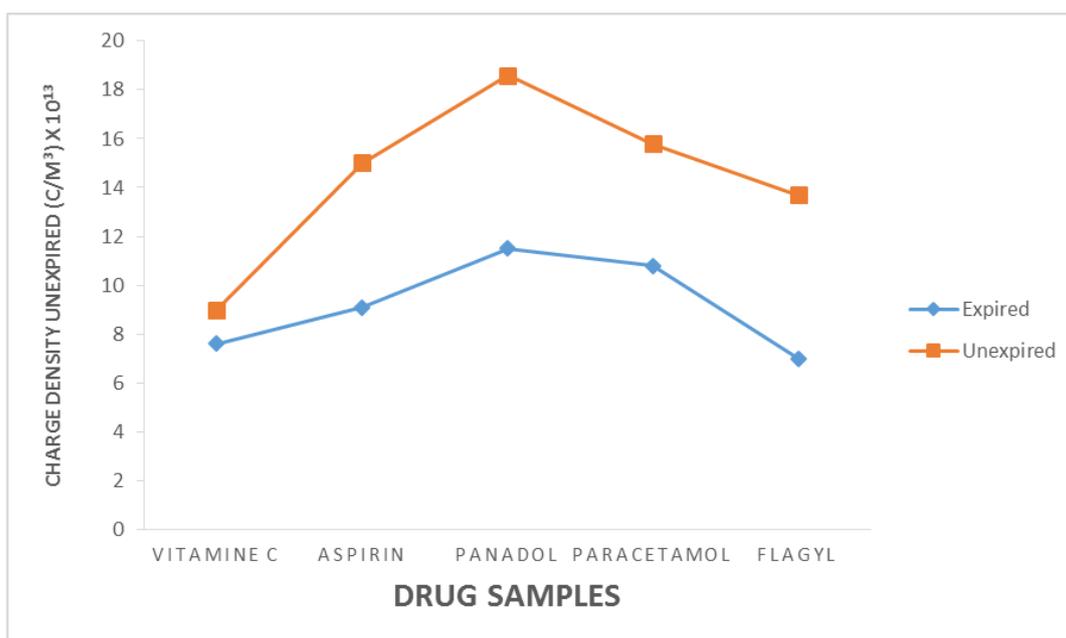


Fig. 3: Bar Chart showing Charge density distribution in different drugs Samples.

The results obtain for conductivity pH and charge density of unexpired and expired drugs are shown in Tables 1 and 2, respectively. A graphical representation of the conductivity, pH and charge density of expired and unexpired drugs samples is shown in Figures 1, 2 and 3 respectively. From Figure 1, 2 and 3, for the unexpired drugs; a maximum and minimum value of 35.66 ± 0.35 and 17.29 ± 0.24 $\mu\text{S/cm}$ for conductivity, 7.80 ± 0.26 and 6.55 ± 0.17 for pH measured at a concentration of $0.5 \text{ g}/100 \text{ cm}^3$ and 18.6×10^{13} and $9.0 \times 10^{13} \text{ C/m}^3$ for Charge density. While the expired drug samples, have a maximum and minimum value of 22.15 ± 0.17 and 13.38 ± 0.22 $\mu\text{S/cm}$ for conductivity, 11.15 ± 0.17 and $5.58 \pm$

0.24 for pH measured at the same concentration and 11.5×10^{13} and $7.0 \times 10^{13} \text{ C/m}^3$ for charge density.

The relatively high conductivity value of the unexpired drugs shows the large number of ions available in the conduction process leading to absorption by the body fluids, while the relatively low conductivity values of the expired drugs sample show that it will take longer time for them to be absorbed by the body cells (Xun and Wattong, 2007). Furthermore, the effect of conductivity on drug is to enhance the absorption of ion by the body cells and performing its healing effect. Thus, low conductivity reduces the rate at which the drug can penetrate the body cells for possible repair thereby

delaying the healing effect (Shanmugamurthy L, *et al.*, 2015).

Normal pH of the human body should be around 7.35 to 7.45. When the pH is higher than this, it results in decreased in cells functionality such as protein synthesis, mineral absorption and many other depending on the very specific pH to function. When the pH gets outside the optimal range, protein synthesis can slow down drastically or completely stop (Lauren 2008). The expired drugs went beyond the range pH value limit of the Human body which poses health threat. A higher pH signifies greater alkalinity and low pH signifies acidity and when the acidity level is high it connotes imbalance pH and can be linked to health issues, such as, heart ailments and cancer (Lauren 2007).

The charge density values obtain in this study as showed in Figure 3 is very low indicating that the amount of charge required in the conduction process of the human body system need not be high. Furthermore, the data obtain for charge density of expired drugs is low compared to unexpired drugs.

CONCLUSION

This study has shown that, electrical conductivity, pH and Charge Density of drugs can be used as a parameter to characterise and monitor the quality of drugs especially commonly used drugs with a view of detecting expired samples and to create awareness in detecting quality deterioration and adulteration of the drugs, other physical and chemical method of determining quality of drugs should be researched into as means of enhancing quality of drugs, since most of the equipment used by drugs quality monitoring bodies (e.g NAFDAC in Nigeria) is either expensive or not portable. This study of analysing expired drugs product is cost effective since it can perform in a simple chemical laboratory.

Awareness should be created in detecting quality deterioration and adulteration of other drugs, so that a database can be kept for referencing

7. REFERENCES

1. XUN, M. and WUTNG, W. Anti biotic effect of an alpha – glucan from fruits body maitake (*Grifola frondosa*) on KK-AY mice. *The journal of pharmacy and pharmacology* 59C4), 2007; 575-82.
2. Lauren, B. Danger of Expired Drugs http://www.livinghelthy360.com/home/Pharm_educational_Prescription_and_medication. (Retrieved 17th March, 2015), 2008.
3. FDA: expiration Date and Stability Testing for Human Drugs Products. <http://www.Scholarshipinindia.com/answer/expirydateinmedicines>. <http://www.vhparmsci.com/vhformulary/policies/5.6>. Expiry dates of Sterlic- pharmaceuticals.
4. Maes, R. A Buformin Concentration in a case of fetal lactic acidosis, 1998; 20(1): 45-6.
5. Stedman's Medical Dictionary. Retrieved via drugs.com, 2017.
6. Lenntech BV Distributieweg 3 2645 EG Delfgauw, Water Conductivity <https://www.lenntech.com/applications/ultrapure/conductivity/water-conductivity.htm> Retrieved, 2017.
7. Shanmugamurthy L, Gaurav K, Pinar A, Rakkiyappan C, Magesh S, Ana E, and Michael R., Physical Energy for Drug Delivery; Poration, Concentration and Activation doi: 10.1016/j.addr.2013.05.010. HSS public Access, 2015; 98-114.