JCBPS; Section C; February 2018 – April - 2018, Vol. 8, No. 2; 102-109, E- ISSN: 2249 –1929
[DOI: 10.24214/jcbps.C.8.2.10209.]

Journal of Chemical, Biological and Physical Sciences

An International Peer Review E-3 Journal of Sciences

*Available online at*www.jcbsc.org

Section C: Physical Sciences

CODEN (USA): JCBPAT Research Article

Expiry date calculations of drugs and cans of foods industry

Talib F. Abbas

Department of Neurophysiology, Faculty of Pharmacy, University of Al-Muthanna , Iraq

Received: 02 April 2018; **Revised:** 11 April 2018; **Accepted:** 18 April 2018

Abstract: Shelf life or stability testing is a main part of quality preserve for many foods and drugs. Biopharmaceutical products in storage change as they age, but they are considered to be stable as long as they keep their characteristics within the manufacturer's properties. Thus one can view shelf-life tests as no special category of sensory testing using accepted methods. The objective of the study may dictate what method is most suitable to answer the research questions. Therefore, the Arrhenius equation is the formula of choice to predict the Shelf life. Unfortunately, not all deterioration processes is equally accelerated by an increase in temperature, foods containing high amounts of lipids, pigments and vitamins are highly relevant to deteriorate by light or radiation rather than temperature. In order to facilitate the use of both temperature and light in an ASLT study, the combination of both accelerating factors light and temperature was deduced into one equation. The Arrhenius equation was substituted into the Power Law equation by simply added the regression value of illumination. Alternatively, D&A used the break angles to calculate the predictive values of shelf life in polymer material sterilized by radiation. The experimental protocols used are similar to the protocols used with the Arrhenius equation.The Q10 factor is based on the Arrhenius equation. Statistical tests indicated that the use of this equation was appropriate with some modulation. Shelf-life predictions were also verified by real-time stability testing results.

Keywords: Shelf life, Arrhenius equation, Pharmaceutics, Food industry.

INTRODUCTION

Shelf life or stability testing is a main part of quality preserve for many foods. It is an inherent part of packaging research because one of the primary functions of food packaging is to maintain the integrity of food in its structural, chemical, microbiological and sensory properties. For many foods, the microbiological integrity of the food will determine its shelf life, and this can be estimated using standard laboratory practices. Processing parameters are expressed in terms of a series of symbols of which D,Z curve, and F value. Hence, one minute is required to reduce the survivors from 1,000 to 100 per gram of food and so on until only 0.01 of a spore is present in 1 gram of food. This time to reduce the survivors by 90% is the Decimal reduction (D) value. The slope of this curve is called the z value. The F value for a process is the number of minutes required to kill a known population of microorganisms in a given food under autoclaving. This F value is usually set at 12 D values to give a theoretical 12 log cycle reduction of the most heat-resistant species of spores in a can of food[1].

Shelf life testing may employ any of the three major kinds of sensory tests, discrimination, descriptive, or effective, depending on the goals of program. Thus one can view shelf-life tests as no special category of sensory testing using accepted methods. The objective of the study may dictate what method is most suitable to answer the research questions[2].

Biopharmaceutical products in storage change as they age, but they are considered to be stable as long as they keep their characteristics within the manufacturer's properties. The number of days that the product remains stable at the recommended storage conditions is referred to as the shelf life. The experimental protocols commonly used for data collection that serve as the basis for estimation of shelf life are called stability tests[3]. The loss of food quality for most food can be represented by mathematical equation,

$$\text{Rate} = -\frac{dA}{d\theta} = KA^n$$

Where,

A=The quality factor measured, Θ= time, K= constant that depend on temperature and water activity.

n= power factor.

In terms of Shelf life, this become equation

$$\theta = \frac{A_0 - A_e}{K}$$

A_o = initial (zero time) value of the quality factor.

A_e= Value of the A at the end of shelf life.

When a new drug product is being formulated, it is desirable to determine the stability, so that a shelf life or expiration date may be assigned to the product.

REAL-TIME STABILITY TEST

The most accurate prediction of shelf life is achieved by full length storage tests under normal storage conditions, which is called Real-time stability test. However, the duration of the test period should be long enough to allow significant product degradation and to distinguish between the percent degradation and long term assay variation. Problems occur when products control are not available as references. Full length storage tests do not only demand a considerable investment in time, but they are also expensive. One approach is to accelerate the shelf life by the increase of some environmental factor, and then using a kinetic model to predict the actual shelf life[4]. The shelf-life is the length of time required for the product potency to be reduced to some percentage of its original value. For most products, this is the T_{90} or time at which the product retains 90% of its original potency.

ACCELERATED SHELF LIFE TESTS (ASLT)

ASLT refers to any method evaluating long-term shelf life of food products on the basis of short-term tests. To achieve this goal, food product is exposed to environmental factors (temperature), and the result is mathematically converted into normal storage conditions. Any storage condition may be altered as long as the following deterioration process can be measured accurately and evaluated by a valid kinetic model by the Arrhenius equation[5].The use of the Arrhenius model is generally accepted and has proven experimental validity [6].

Unfortunately, not all deterioration processes is equally accelerated by an increase in temperature, the problem that arise when the reaction causing the quality deterioration has alow thermal activation energy. Foods containing high amounts of lipids, pigments and vitamins are highly relevant to deteriorate by light or radiation rather than temperature[7].

Most ASLT studies is performed using temperature as the single accelerating factor, and the most common way of describing the rate of deterioration in relation to temperature is by the Arrhenius Equation

$$K = K0 \exp\left(-\frac{Ea}{RT}\right)$$

Where,

k= the reaction rate constant expressed in kJ/mol K,

$k0$=the Arrhenius equation constant,

Ea=denotes the activation energy in kJ/mol,

T=represent the absolute temperature expressed in Kelvin

R =the universal gas constant of 8, 3144 J/mol K

The activation energy (Ea) is given by eq.

$$lnK = lnk0 - \frac{Ea}{R\left(\frac{1}{T}\right)}$$

Ea can also be found by plotting ln(k) versus 1/T in a graph as shown in **Fig.1**

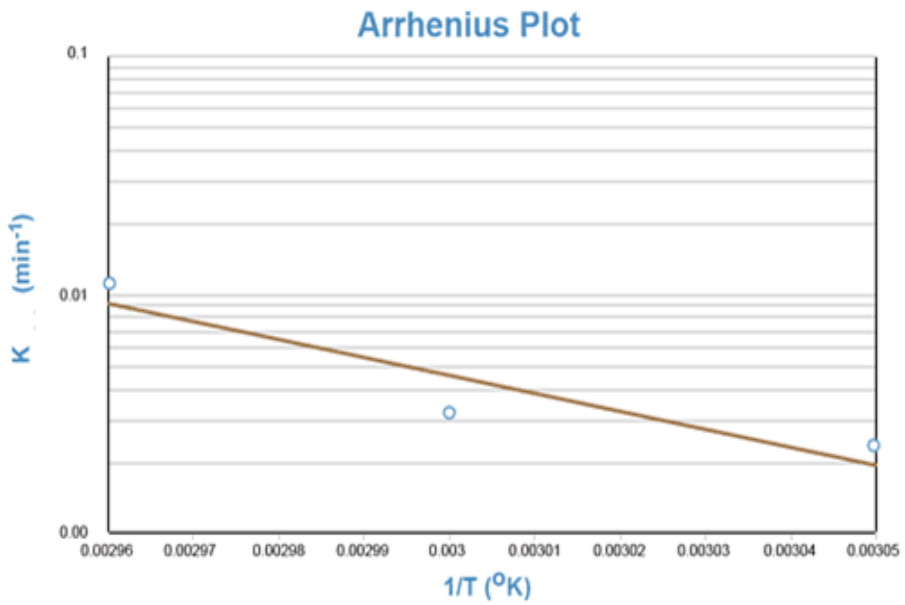


Fig.1: show the Arrhenius plot graph to calculate the activation energy.

According to Manzocco *et al.*[7] the activation energy for most food may range from 2-5 kJ/mol to 300-400 kJ/mol, and a low activation energy (*Ea*<50 kJ/mol) refer to a scarce temperatures dependence. If a food product has low temperature deterioration, high temperature will not increase in reaction rate of the spoilage. For high *Ea*(>50 kJ/mol), the opposite is true and the reaction rate of the deterioration marker will increase with elevated temperatures.

ASLT studies are often performed at temperatures 10 °C apart, which enables the so called Q10 – factor to be calculated from equation

$$Q_{10} = \frac{\text{rate of loss of quality at temperature (T + 10°C)}}{\text{rate of loss of quality at temperature T °C}}$$

kT + 10 and *kT* denotes the rate constants.

From this relationship, an alternative way to calculate the activation energy by using equation

$$\ln(Q10) = \frac{10Ea}{RT}$$

One of the advantages of using Q10 lies in the fact that the activation energy can be calculated using only two separate measurements. The method is also fairly straightforward. The *Q10* – factor helps predict the time-temperature relationship from ASLT tests, and in

order to convert the result into normal storage condition temperatures the Q10 factoris needed. If the *Ea*is known, *QF* is calculated from equation

$$QF = \exp\left[\frac{Ea}{R\left(\frac{1}{Ts} - \frac{1}{Te}\right)}\right]$$

Where, *Ts* = Actual (user) storage temperature in K, and *Ts*= test temperature in K. Once the *QF* is known, the Shelf time (*ST*) can easily be found by multiplying the number of days before the cutoff point is met by the *QF*

$$ST = \exp\left[\frac{Ea}{R\left(\frac{1}{Ts} - \frac{1}{Te}\right)}\right]t$$

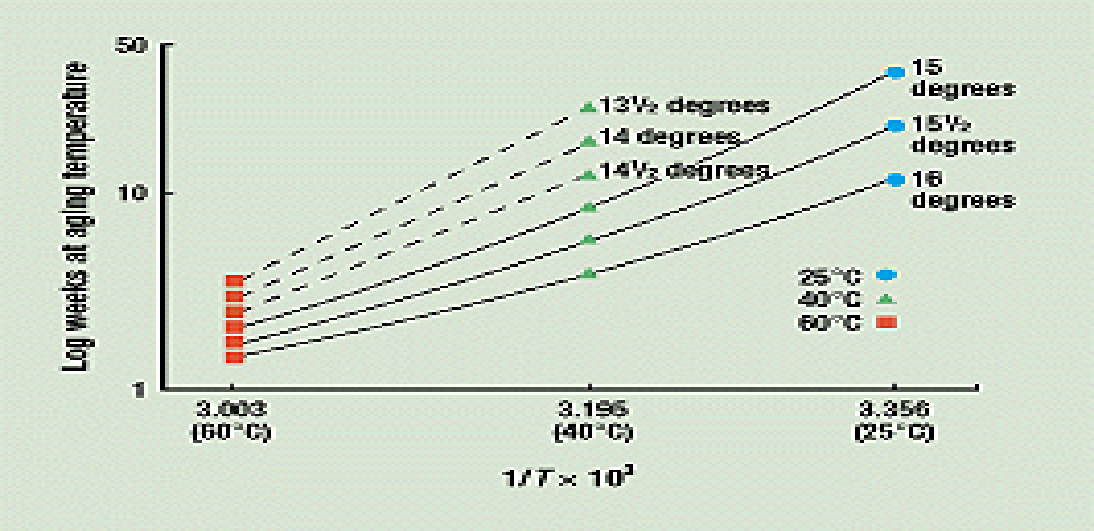
In order to ensure that the confidence limits are narrow, at least five or six different temperatures are recommended for the Arrhenius equation, while the *Q10* – modeling only requires at least two different temperatures[8].

PREDICTING SHELF LIFE FOR MEDICAL DEVICES

The medical device industry has long been interested in techniques for predicting the shelf life of polymer-based devices. Many polymers important to the medical device industry are damaged by the radiation required to sterilize them, darkness as in polypropylene), discoloration (as in polycarbonate), however, the chemical damage will not break when the radiation stop; it continue in dark reaction often years. Thus, the rates of chemical reactions, within the limits of certain restrictions, increase with temperature, as described by the Arrhenius equation will not lead to true predication of shelf life. The dark reaction that irradiated polypropylene is the degradation of peroxides that are formed by radiation-induced free-radical oxidation which is not accurate representative of Ea for peroxide decay.All these complications ensure that giving data will not follow the Arrhenius equation[9].

Given all these heterogeneous effects, it's clear that even the chemical reactions that are being accelerated can be expected to deviate from the Arrhenius equation. In addition, physical complications must be accounted for. The curve line will be not straightforward between the K value and 1/T, it appeared a curved yield. The correction method is the break angels as used by D&A methods, by using the curvatures of the three sets or more of data; it will be possible to make a predictable curve depending on break angles of curvatures as shown in the **Figure 2.**

In order to facilitate the use of both temperature and light in an ASLT study, the combination of both accelerating factors light and temperature was deduced into one equation by Manzocco *et al.*[7]. The Arrhenius equation was substituted into the Power Law equation by simply added the regression value of illumination.



Fiq. 2: show theSolid lines show aging time for samples in each of the three storage temperatures to reach break angles of 16, 15½, and 15 degrees. The broken line indicates the time for the samples stored at 40° and 60°C to reach break angles of 14½, 14, and 13½ degrees.(Karl Hemmerich and James Stubstad calculations in FDA Guideline[10]).

APPLICABLE EXAMPLES AND PROBLEMS

A common practice in industries is to extract various shortcuts, e.g. bracket table and Q value to estimate the shelf life. The prediction may estimate only by using a few stressed samples. However, they are based on assumptions that the activation energy of product as less as 10 and as high as 20. Whatever method is chosen, the validity of product stability projection depends on analytical precision, the valid control specimens, and accurate mathematical model and formula.

The bracket method is a straightforward application of the Arrhenius equation that can be used if the value of the activation energy is known, the degradation rate at storage temperature may be predicted from data collected at only one elevated temperature. Assuming that stability of a product at 50°C is 32 days, and it will be stored at 25°C, then, t_e = 32 days, T_e = 273 + 50°C = 323K, and T_s = 273 + 25°C = 298K. We know that activation energy is E_a = 10 kcal/mol. Stability at recommended storage temperature is calculated with a modified version of Equation:

$$K = \exp\left[\frac{Ea}{0.00199\left(\frac{1}{Ts}-\frac{1}{Te}\right)}\right]te$$

=exp[10/0.00199(1/298-1/323)]23= 118 days.

The Q-Rule states that the degradation rate decreases by a constant factor when temperature is lowered by 10 °C. The value of Q is typically set at 2, 3, or 4 because these correspond to

reasonable activation energies. This factor is proportional to the temperature change as Q^n, where n equals the temperature change in °C divided by 10°C. Since 10°C is the baseline temperature, the Q-Rule is sometimes referred to as Q_{10}.

To illustrate the application of the Q rule,let us assume that the stability of a product at 50°C is 32 days. The storage temperature is 25°C and n = (50 - 25)/10 = 2.5. Let us set an intermediate value of Q = 3. Thus, $Q^n = (3)^{2.5}$ = 15.6. The predicted shelf life is 32 days * 15.6 = 500 days. This approach is more conservative when lower values of Q are used. A Q10 value of 2 provides a conservative estimate, and results calculated with this value are considered probable. A Q10 value of 4 is less conservative and yields results considered to be possible[11].

DISCUSSION

In Australia and New Zealand, canned foods that have a shelf-life of less than two years require a 'best-before date' (date mark) on the label. Canned foods with a shelf-life of more than two years do not need a 'best before' date. These foods do not carry a date mark as it is very difficult to determine a meaningful date when the shelf life is two years or longer. While canned foods do not change suddenly, slow changes do occur in the container and food quality may change over time. The storage life depends on a number of factors, including conditions of storage and the nature of food. As a general rule, the best shelf life will be obtained when canned foods are kept in a cool, dry place[12].

The temperature inside the containers during heat treatment must be measured at the "coldest" or critical thermal point of the product, which is the point where the heat transferred through the centre of the container (can). This situation also implies that the outer parts of the canned product always receive higher amounts of heat treatment than the centre. The F-value required for a product must be reached and measured at the critical thermal point (cold point). This fact plays a role in the sensory quality of the product. The sterilization process must therefore be carried out in a way that also the outer product portions are not deteriorated by excessive heat treatment and are acceptable to consumers both in texture and taste.

Refrigerated products are widely used, their projected stability deduced exclusively at 5°C degradation rate. Shelf life depends on the activation energy which is in assumption mode for product between 10 and 20 kcal/mol, because the product is not one molecule in content. The stability test cannot apply with one attempt of stress temperature[13].

Simple linear regression analysis seems to be good method if the temperature is only retardation factor in food and drug spoilage. Nevertheless, the medical advice and many industrial products have used the radiation which plays as accelerated factor in retardation. Light also considered to be affecting factor in pigmented stored products which may add more complexity to the predicting equations[7]. Arrhenius analysis permit weighted least squares statistical treatment and produces a valid projection stability. The optimization the ASLT design, it will expect accelerated stability values to provide more valid information.If the degradation patterns of the test and control samples at the same elevated temperatures are not statistically different, it can be assumed that they will degrade similarly at the storage temperature. The experimental protocols used are similar to the protocols used with the Arrhenius equation. The Q10 factor is based on the Arrhenius equation. Statistical tests

indicated that the use of this equation was appropriate in this case with some modulation. Shelf-life predictions were also verified by real-time stability testing results.

REFERENCES

1. S.H.Hekeem & M.H.Abid Ali, Food Industry, 1st part, Baghdad Press.1985, Iraq.
2. P.Fellows, Food Processing Technology Principles and Practice. Sec. Ed. CRC Press. BoCa Raton Boston New York Washington, DC, 2000.
3. J.F.Norwing and D. R. Thompson, Microbial Population, Enzyme and Protein Changes during Processing. In Physical and Chemical Properties of Food , MR Okos ,Ed. St. Joseph , MI. : American Society of Agricultural Engineers , 1986, 202 – 265
4. A.A.Teixeirn and G. S. Tucker. On – Line Retort Control in Thermal Sterilization of Canned Foods. Food Control, 1997,(8): 13 – 20.
5. G.Hough, Sensory Shelf Life Estimation of Food Products. Boca Raton: CRC Press, Taylor & Francis Group, 2010.
6. S.Mizrahi, Accelerated shelf life testing of foods. In: Kilcast, D., &Subramaniam, P. (ed.) *The Stability and Shelf Life of Food*. Woodhead Publishing Limited, 2011.
7. L.Manzocco, A.Panozzo, &S.Calligaris, Accelerated shelf life testing (ASLT) of oils by light and temperature exploitation. *Journal of American Oil Chemists' Society, 2012*,89, 577-583.
8. *"US Army Medical Materiel Agency (USAMMA)". Usamma.army.mil. 2013*.
9. K.T.Gillen,R.L.Clough andJ.Wise, .Extrapolating Accelerated Thermal-Aging Results: A Critical Look at the Arrhenius Method, in *Polymer Preprints*, Washington, DC, American Chemical Society, 1993, 34(2):185.
10. FDA, Guidelines for submitting documentations for the stability of human drugs and biologics. Rockville (MD); Maryland: Food and Drug Administration, Center for Drug and Biologizes, Office of Drug Research and Review, 1987.
11. K.A.Connors, G.L.Amidon, L.Kennon, Chemical Stability of pharmaceuticals-a handbook for pharmacists. New York: John Wiley & Sons, 1973, 8, 119.
12. W.Andrew, Manual of Food Quality Control. 4- rev. 1 . Microbiological Analysis .FAO Food and Nutrition Paper .1992,4 / 4 (rev. 1)
13. R.T.Toledo, Fundamentals of Food Process Engineering. 3ed. Spring Sci. +Business Media, LLC.2007, 589.

*** Corresponding author: Talib F. Abbas,**

Department of Neurophysiology, Faculty of Pharmacy, University of Al-Muthanna , Iraq

Online publication Date: 18.04.2018