Equilibrium Moisture Sorption Isotherms of Aspirin

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ABSTRACT:

Equilibrium Moisture sorption isotherms are very important in drying and storage analysis. Experimental moisture equilibrium data (adsorption and desorption) of Aspirin were determined using the static method of saturated salt solutions and that by exposing the material to different conditions of temperatures and water activities. Three different temperatures (25, 30, 40Cº) and water activities in the range of (6.3- 83.6%) were used.

The results showed that the equilibrium moisture content increased with the increase in water activity at any temperature and decreased with temperature increase at constant water activity. The water activity increases with increasing in temperature when moisture content was kept constant. The sorption isotherm curves are of type II according to Brunauer`s classification. The hysteresis effect was not distinctly expressed only for equilibrium sorption values of Aspirin at 25ºC. The experimental results were fitted to two sorption models (GAB and Henderson).The average relative deviation between the experimental and calculated data were obtained to select the best model. The GAB and Henderson models, obtaining values of 3.54 and 1.42 % average relative deviation and coefficient of regression of 0.98 and 0.977 respectively. The Henderson model was found to be the best fit out of the two models to predict the sorption behavior of Aspirin.

Keywords: Equilibrium moisture content, Water activity, sorption isotherms, Mathematical modeling, pharmaceutical, Aspirin.

الخلاصة :

ان دراسة منحنيات محتوى الرطوبة عند الاتزان لكل من حالتي الامتزاز والأد-امتزاز مهمة في تحليل ودراسة الظروف المناسبة للخزن واختيار ظروف وطريقة تجفيف المواد خاصة المواد الحساسة مثل الاسبرين.

تم الحصول على النتائج العملية باستعمال طريقة المحاليل الملحية المشبعة وذلك بتعريض المادة الى ظروف مختلفة من درجة الحرارة وفعالية الماء (الرطوبة النسبية عند الاتزان) . تم استعمال ثلاث درجات حرارية مختلفة (40,30,25) درجة سيليزية وفعالية الماء في المدى (6.3- 83.6%) .

اوضحت النتائج العملية ان محتوى الرطوبة عند الاتزان يزداد مع زيادة فعالية الماء عند اي درجة حرارية، ويقل مع زيادة درجة الحرارة بثبوت فعالية الماء. والأخيرة تزداد مع زيادة درجة الحرارة بثبوت محتوى الرطوبة .الهسترة لم تكن واضحة فقط عند درجة حرارة 25. إ ن المنحنيات في الحالتين هي من النوع الثاني حسب تصنيف العالم برونير. تم تحليل النتائج العملية ومطابقتها مع موديلين رياضيين هما (كوكنهام- أندرسون ودي – بور) وهندرسون . نسبة الانحراف النسبية للموديلين 3.54 و 1.42 % ومعامل التطابق 0.98 و 0.977 % ، حيث وجد ان موديل هندرسون أفضل في تمثيل الايزوثيرم للاسبرين.

INTRODUCTION

The knowledge of equilibrium moisture isotherm is very important in storage and drying processes analysis. During the storage and drying of products, physical and chemical changes occur; these changes are particularly influenced by moisture content of a material, relative humidity and the storage and drying conditions. (Motta L., et al., 2004)

The water sorption isotherm of a material shows the equilibrium relationship between the relative humidity and the moisture content of a material (expressed as mass of water per unit mass of dry material) at constant temperature and pressure (Maria L. et al., 1993). Thus with the knowledge of the moisture isotherm it is possible to predict the maximum moisture that the material can be allowed to gain or loss during storage. The adsorption isotherms data can be used for a storage method determination and while the desorption data can be used for drying analysis. (Daniel S. et al., 2004)

Water is an important component of nearly all materials and plays a decisive role in dictating the degradation of a material. For most materials, much of the water content is freely available to behave physically as pure water with properties such as vapor pressure equal to pure water; As moisture content is lowered, a point will be reached at which the water becomes less active, in that it can not act physically or chemically as pure water, in this state, it is considered to be bound water .Thus, the amount of free water rather than the amount of total water is critical to the chemical and physical stability of a dry substance that is moisture sensitive (Bags K. et al.2009).

When a sample comes into equilibrium with the atmosphere surrounding it, the water activity in the sample becomes equal to the relative humidity of the atmosphere surrounding it or in which it is stored. Once this equilibrium is reached, the sample neither gains nor loses moisture over time. The moisture uptake/loss rate depends on the relative humidity of the environment and the time (Mark J. et al., 2006).So the water activity a measure of the free water in a pharmaceutical dosage form (Bell L.,2000).

The relationship between water content and water activity is complex. An increase in water activity is almost always accompanied by an increase in the water content, but in a non-linear relationship. These isotherm curves are determined experimentally (Bell L., 2000), and they are important to determine the stability criteria for pharmaceuticals which their properties are critically dependent on the presence of moisture (Mark J.et al., 2006). Water in pharmaceutical products either as the residual water from processing or as the result of exposure to high relative humidity may affect the chemical and physical stability of moisture sensitive products (Yanxia L. et al.,2003). The stability is a critical quality of pharmaceutical products and it varies with time under the influence of a variety of environment factors; such as; temperature, humidity, light, and others. So these curves can be used to help predict product stability over time in different storage conditions or drying processes (Kim H., 2001). The free water content and therefore degree of water activity provides more valuable information than the total moisture content when considering the stability of moisture sensitive products (Cunningham C. et al., 2001).

Water activity, is unitless and the values of unity indicates pure water where as zero indicates the total absence of water molecules ($0< a_w< 1$), is defined as the ratio of vapor pressure of water in the material to the vapor pressure of pure water at the same temperature (Bob S. et al., 2007):

$$a_w = \frac{p}{p_o} \qquad (1)$$

Equilibrium relative humidity is water activity expressed as a percentage:

$$ERH = a_w \times 100 \qquad (2)$$

Since the vapor pressure of water is strongly dependent upon temperature, then the water activity is temperature dependent, it follows that temperature has a significant effect on sorption isotherms. so when a material is subjected to an upward temperature shift, at any moisture content, water activity increases with increasing temperature .Thus both temperature and relative humidity must be specified to determine the total amount of water available during the sorption process(Yihong Q. et al.,2009).

The study of whether water will adsorb or desorb from a particular component is essential to prevent degradation, especially if the substance is moisture sensitive. For example, two separate materials (initially at different water contents and water activities) stored at 25% relative humidity, will reach a water activity of 0.25, although the final water content of the two materials will be different. If the materials are moved to a higher or lower relative humidity then the water will increase or decrease, respectively until equilibrium is reached. Likewise, if two materials of differing water activities and the same water content are mixed together, then the water will adjust between the materials until equilibrium water activity is obtained. Therefore, water activity over water content provides useful information for formulation design, manufacturing conditions and packing requirements. Many disciplines use water content calculations to regulate product quality, however, water content measurement can be inaccurate and time-consuming, especially for pharmaceuticals, a particular compound has a water content of 0.05% and measuring water content in this range is difficult and requires a precision balance. For this compound, changes as small as 0.02% in water content corresponded with a 0.2 change in water activity, clearly, the water activity measurement permits much tighter control of the products specifications (Martin C.,2009) . The drying equipment is designed to remove moisture, and only moisture content can be measured and controlled on the factory floor (not water activity). The sorption isotherm becomes the fundamental tool by which it is possible to specify the moisture content needed that will assure the required water activity of a pharmaceutical solid with optimal properties. (Anthony J. et al. , 1999). Many researches have developed to study and model the equilibrium moisture content of food but very few of pharmaceuticals (Daniel S. et al., 2004).

Aspirin, some times known as acetylsalicylic acid, is the salicylate ester of acetic acid, is the most widely used drug in the world, no other drug in the history of medicine has exhibited such an array of multifaceted therapeutic properties (Alexander G., 1998). Aspirin is moisture sensitive and considered as a hygroscopic material (Hygroscopicity is a term used to describe how readily a material will take up moisture when subjected to a given change in relative humidity). (Charles R. et al.2004).

The compound is a white, crystalline powder or tabular or needle like crystals. It is a weak acid. Aspirin tablets should be stored in tight, moisture resistant containers. It is stable in dry air, but readily hydrolyzes to acetate and salicylate when exposed to moisture air, the addition of heat will speed the rate of hydrolysis (Susan K. et al., 2003). The deterioration may take several forms: It can be physical deterioration in which aspirin compositions become completely unmanageable, wet, gummy, sticky masses, or chemical decomposition in which Aspirin loses its molecular structure, or may degrade to a toxic substance (Sumie Y.et al., 2008). In both cases, such composition becomes unsuitable for all practical commercial and medicinal purposes (Alexander G., 1998).

The experimental equilibrium data were obtained by using the classical methodology of exposing the solid material to different conditions of temperature and relative humidity (Motta L. et al., 2004). This method is called the static method or the gravimetric technique, in which, the sample brought in to equilibrium in a closed system of known constant relative humidity. All classical methods require either temperature stability and uniformity or accurate measurement of the temperature (Wolf W. et al., 1985).

The relative humidity was controlled by saturated salt solutions. The value of the relative humidity depends on the salt used. The salts were chosen to obtain a large range of relative humidity (6.3- 83.6 %). The method is widespread as humidity generators because of the ease of handling, low cost of salts and the ease of maintenance of the humidity conditions with high accuracy, but it is labor-intensive and time - consuming until equilibrium is reached between the material and water vapor (Jiri B. et al., 2008).

The objective of this study is the determination of the adsorption and desorption isotherms of Aspirin, at water activities ranging from 6.3- 83.6 and temperatures of 25, 30 and 40 ºC. Two models: GAB and Henderson were fitted to the experimental data in order to describe the equilibrium moisture sorption isotherms of Aspirin.

EXPERIMENTAL PROCEDURE

Material:

Aspirin, produced by Samarah Drug Industry (SDI) was used. For adsorption process the material was with a final moisture content of 1.5%, and for the desorption process a wet material was used with an initial moisture content of 19%.

Method:

The method of preparation of saturated salt solutions was as follows:

Pure salts and distilled hot water in the proportions shown in table (1) were mixed with stirring, excess salt should then be added. The final solution was cooled and allowed to stand a few days at the desired temperature in closed conditions. The solution should be stirred once a day using magnetic stirrer to assure the right formation of the saturated salt solutions. Solutions are made at a higher temperature than equilibration to ensure that they are saturated when cooled. (Shyam S. et al., 2001).

Table 1: preparations of saturated salt solutions at 25ºC (Greenspan, 1977)

Salt kind	Relative Humidity (%)	Distilled Water (ml)	Salt (gm)
LiCl	11.3 ± 0.27	75	42.5
NaOH	8.9 ± 0.7	100	36
$MgCl_2$	33.07 ± 0.18	100	12.5
K_2CO_3	43.16 ± 0.18	100	45.0
$Mg(NO_3)_2$	54.4 ± 0.23	100	15.0
NaBr	59.1	100	40.0
KI	69.9	100	25.0
NaCl	75.47 ± 0.14	100	30.0
KCl	84.34 ± 0.48	100	40
kBr	80.9	100	32

The temperature might affect the relative humidity promoted by the saturated solutions; this effect was considered in the correction of the solutions relative humidity values used in the construction of the isotherms curves (Motta L. et al, 2004).The correction is shown in table (2).

Table 2: correction of relative humidity with temperature (Greenspan, 1977)

Salt Solution	Temperature ºC		
	25	30	40
	Relative Humidity		
NaOH	8.9	7.6	6.3
LiCl	11.3	11.3	11.2
$MgCl_2$	33.1	32.5	31.6
K_2CO_3	43.2	43.1	43.0
$Mg(NO_3)_2$	54.4	51.4	48.4
NaBr	59.1	56	53.2
KI	69.9	67.9	66.1
NaCl	75.5	75.1	74.7
KCl	84.82	83.6	82.3
kBr	80.9	80.6	79.9

A glass desiccators, containing the salt solutions, were tightly sealed from the outside atmosphere, their covers are designed in such away that can by easily opened and re-closed quickly for removal of the samples during the few minutes required for periodic weighing. The desiccators were kept in a temperature controlled chamber, in an air circulation oven, to ensure that the temperature was constant. The experiments were carried out at three different temperatures (25, 30, and 40 ºC).

The equilibrium moisture contents were determined by a gravimetric technique: Samples of known initial moisture content (of 3g each) were weighted just prior to storage using a standard balance of sensitivity ± 0.0001g (model Sartorius). The samples placed in uncovered crucibles placed over the support inside the tightly closed desiccators, so that they do not enter in contact with the salt solutions. It is important to note that the sample size has a great effect on time required to reach equilibrium because of time needed for diffusion of molecules though the interior structure of the sample, so small sizes are recommended. The sorption process is strongly temperature dependent and the temperature must be kept constant and controlled while all experiments are being carried out, thus, each desiccator with the sample inside it was placed in an electric oven at the desired temperature ± 0.2 ºC and allowed to equilibrate with the environment inside the containers. The samples were weighted and recorded periodically until the percentage of changes between two successive readings was less than 1% to ensure that the equilibrium was reached. The sample had a water activity equal to the controlled constant relative humidity regenerated by the salt solutions. The moisture content of the sample was determined by the oven method (LOD method) at 105 ºC for 24hr (Ludger O. et al., 2003).

To obtain sorption isotherm experimental curves ,moisture content values were measured at provided relative humidity conditions in increasing order ,for the desorption , the same saturated salt solutions were used but in this case in decreasing relative humidity order.

RESULTS AND DISCUSSION

The results of the experimental measurement of the equilibrium moisture content and the respective water activity (equilibrium relative humidity) at three temperatures 25, 30, 40 ºC are presented in Fig. 1, 2, 3. (Some experimental values were not considered).

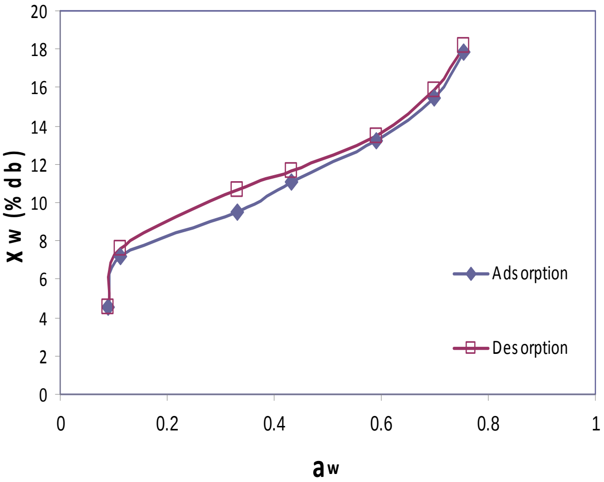

Fig. 1 Experimental moisture sorption isotherms of Aspirin at 25 ºC

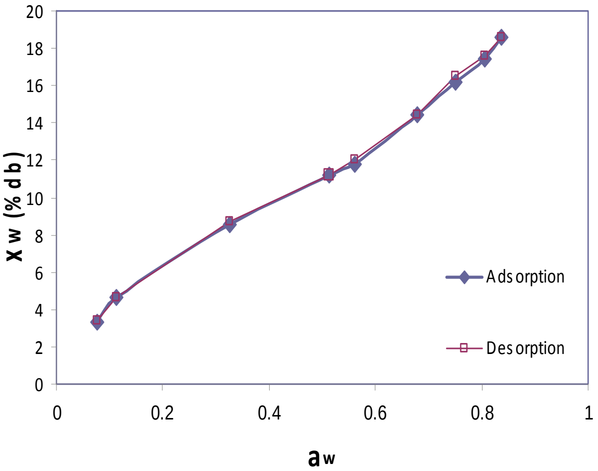

Fig. 2 Experimental moisture sorption isotherms of Aspirin at 30 ºC

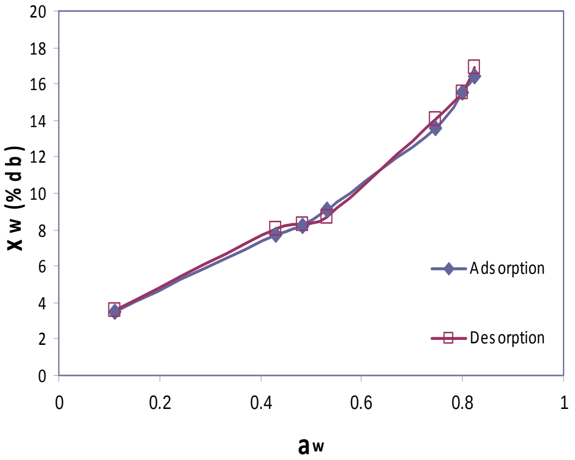

Fig. 3 Experimental moisture sorption isotherms of Aspirin at 40 ºC

There was an increase in equilibrium moisture content values with increase in the water activity at constant temperature, this behavior was observed for both adsorption and desorption curves. (Bell L. , 2000) , (Joseph A., 2009).

The curves can be described by isotherms type II according to Brunauer`s classification (Mark D., 2001), they have sigmoid shape (S-shaped), which is common for many hydroscopic products (Ethman C. et al., 2008), and this can be explained by the changes in equilibrium moisture content are due to an inability of the substance to maintain vapor pressure at unity with decreasing moisture content. As moisture content decrease, moisture in the material tends to show a lower vapor pressure, acting as if in a solution, changing with atmospheric humidity. It is these changes in vapor pressure in the pharmaceutical with atmospheric humidity which result in the characteristic S-shape of water sorption isotherms (Caurie M., 1970).The resulted curves are caused by the combination of effects (physical properties of solution ,capillary effects and surface-water interactions) .A distinct “knee” usually indicates a formation of a well-defined monolayer (Bell L.,2000).

The equilibrium moisture content values for the adsorption process is lower than that of the desorption process at constant water activity, this behavior was analogous to other pharmaceutical (Jhoany A. et al, 2010).

The hysteresis effect was not distinctly expressed only for equilibrium sorption values of Aspirin at 25ºC. By increasing the temperature the hysteresis effect was undergo a reduction in size (Rouquerol F. et al.,1999).Also the shape and width of sorption hysteresis loops were dependent on temperature and type of material (Thommes M. et al.2002). This hysteresis is due to non- reversible structural changes and non- equilibrium effects. (Martin C.,2009); and this can be explained that the principle factors affecting hysteresis are the composition of product, isotherm temperature ,storage time before isotherm measurement ,pretreatments , drying temperature and the number of successive adsorption and desorption cycles. It should be noted that the occurrence of hysteresis indicates either the adsorption or the desorption curve is not at true equilibrium or that some material in the product changed state in the process. (Rahman M. et al., 2000).

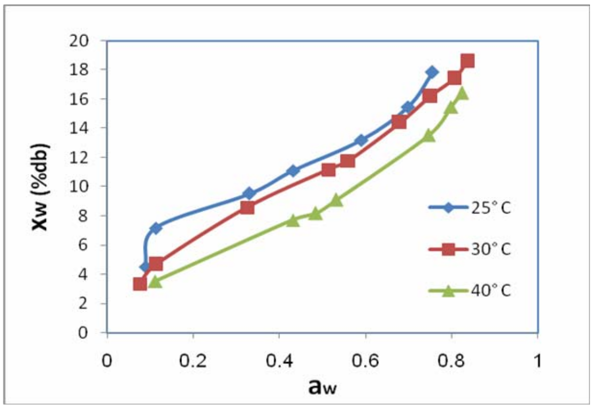

Fig. 4 Adsorption isotherms of Aspirin at different temperatures.

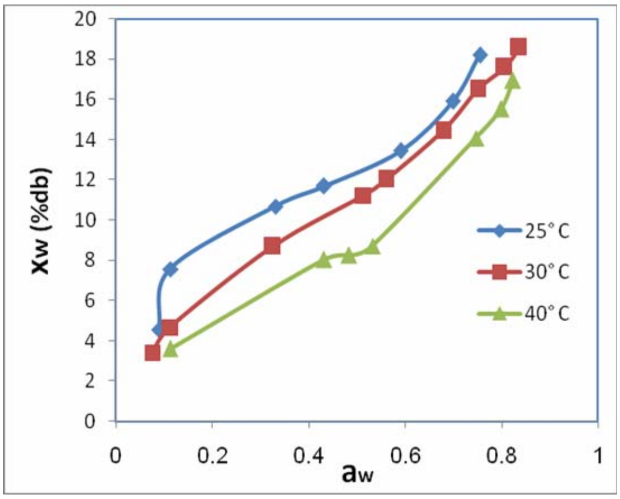

Fig. 5 Desorption isotherms of Aspirin at different temperatures.

As shown in Fig. 4 and 5, temperature has a significant effect on sorption isotherms. The equilibrium moisture content values decreased with an increase in the temperature at constant water activity (Milton C. et al., 2004).This behavior indicates that the material becomes less hygroscopic at higher temperatures (Daniel S. et al.,2004) and this result may be explained that at higher temperatures, the kinetic energy of the water molecules was high and that mean the molecules are in an increased state de excitation, thus increasing their distance apart and decreasing their attractive forces between them, this leads to a decreased in the degree of water sorption at given water activity (Bags K. et al., 2009).This behavior is typical for pharmaceuticals(Acosta J. et al.,2010).

An increase in temperature causes an increase of water activity at the same moisture content, and this is mainly due to the change in the enthalpy of water binding, dissociation of water, physical state of water or increase in solubility of solute in water as temperature increases, which causes of the reaction rates leading to quality deterioration. So the relative humidity had the greater influence compared to other variables (Shyam S. et al., 2001).

At constant moisture content, an increase in temperature caused lowering of isotherm curves making Aspirin more susceptible to degradation (Joseph A., 2009).

The points at low values of water activity (a_w < 0.55) represent the sorption bound water and so isotherm has only a gentle upward slop. As the water activity increases, the equilibrium moisture content increases sharply with water activity due to capillarity. This moisture content can be chosen as a guarantee that the product will be adequately preserved because the water activity is low enough to prevent degradation and also to maintain the moisture content of the product with the desired range of values (Aroldo A. et al., 2004).

FITTING OF SORPTION MODELS TO EXPERIMENTAL DATA

The experimental equilibrium moisture content data at 25, 30, 40 ºC were fitted using two isotherm models namely: Guggenhein , Anderson and de Boer (GAB) and Henderson models. The parameter values were derived from the regression curves of the two models.

The goodness of fit of both models was evaluate and expressed as mean relative percentage deviation (%E) using the equation with value below 5% indicative of a good fit for practical purposes (Menkov D. et al., 2004).

$$\% E = \frac{100}{N} \sum_{i=1}^{N} \left| \frac{x_w - \hat{x}_w}{x_w} \right| \qquad (3)$$

THE GAB MODEL:

The GAB model (Guggenhein , Anderson and de Boer) is a multi molecular sorption model intended for use over a wide range of water activity (up to 0.9) and it is one of the most widely accepted models for sorption isotherms (Jiri B. et al., 2008), and can be written as a three parameter as follows:

$$x_w = \frac{x_m \, c \, k \, a_w}{(1 - k \, a_w)(1 + (c - 1))k \, a_w} \qquad (4)$$

The monolayer moisture content x_m represents the moisture of the material when its entire surface is covered with a unimolecular moisture layer. It is the moisture content for the maximum stability, and it is generally decreased with temperature (Joseph A., 2009).

The parameter k is a factor correcting the properties of the multilayer in the GAB sorption equation varies from unity to zero (0<k≤1) (Jorge C. et al., 1992).

The third parameter C should be higher than zero. For c ≥2, the GAB equation gives a sigmoid shape curve (type II of Brunauer`s classification) (Mark D., 2001).

The parameters $x_{m,}$ c, k are temperature dependent.

The GAB constant obtained by transforming eq. (4) to the quadratic form (Jiri B. et al., 2008):

$$\frac{a_w}{x_w} = \alpha a_w^2 + \beta a_w + \gamma \qquad (5)$$

The coefficients of the polynomial can be determined by plotting a_w/ x_w versus aw and by a non-linear regression fitting procedure using a polynomial of second degree, the coefficients can be determined and then the GAB constants calculated:

$$\alpha = \frac{k}{x_m} \left(\frac{1}{c} - 1 \right) \qquad (6)$$

$$\beta = \frac{1}{x_m} \left(1 - \frac{2}{c} \right) \qquad (7)$$

$$\gamma = \frac{1}{x_m . c . k} \qquad (8)$$

The results of the fitting of the GAB model to the experimental data are shown in Fig. 6,7, and 8 and the constants, the regression coefficient (R^2) and the mean relative percent deviation (%E) are presented in Tables (3) and (4).

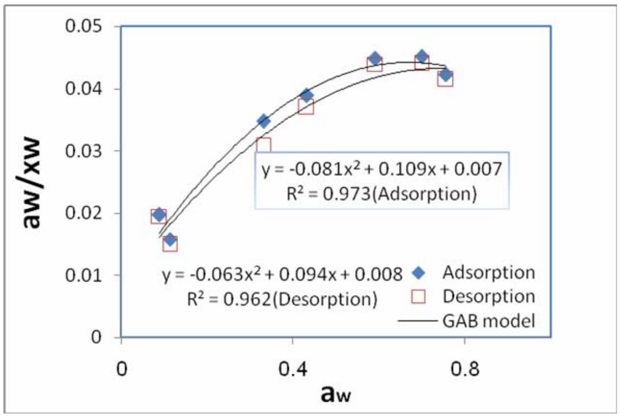

Fig. 6 GAB model isotherm curves for Aspirin at 25 ºC

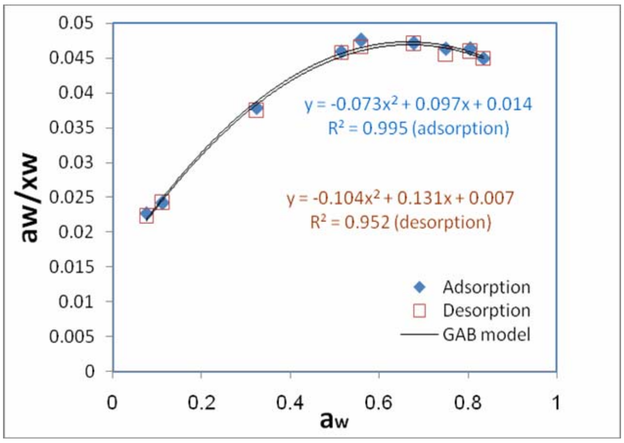

Fig. 7 GAB model isotherm curves for Aspirin at 30 ºC

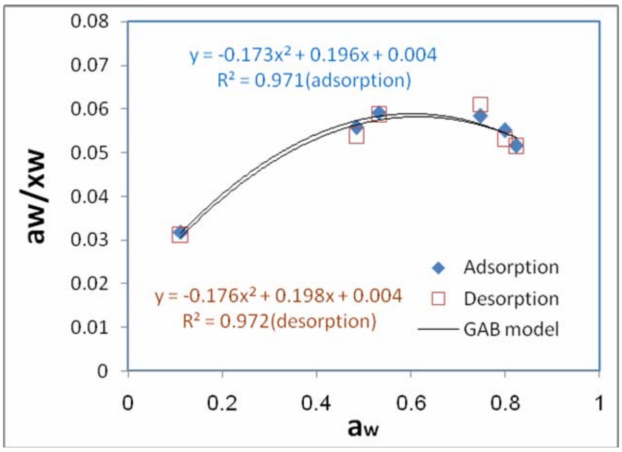

Fig. 8 GAB model isotherm curves for Aspirin at 40 ºC

From the results presented in tables 3 and 4, the GAB parameters are temperature dependent. As the temperature increased from 25 to 40 ºC, the monolayer moisture content x_m decreased from 8.03 to 4.93 for adsorption and from 7.28 to 4.88 for desorption and this behavior was an indication that the adsorbed molecules gained kinetic energy making the attractive forces to be loosened and this allowed some water molecules to breakaway from their sorption sites thus decreasing the equilibrium moisture content value (Aroldo A. et al., 2004).The decrease in the monolayer moisture values (x_m) with increase in temperature was an indication on that the multilayer has properties between these of the monolayer and bulk liquid(Menkov D. et al.,2004).

The range of k values, less than unity, was in agreement with the GAB model assumptions. The constant k increased with temperature from 0.79 to 0.88 for adsorption, and 0.79 to 0.87 for desorption while C decreased from 49.5 to 11.46 for adsorption and 58.25 to 9.72 for desorption , increase in K values was an indication that at higher temperature ,the multilayer molecules became more entropic while a decrease of C was an indication of more enthalpy and a gain in kinetic energy resulting in loss of more moisture at higher temperature(Joseph A.,2009).

The C values are greater than 2 and that with agreement that the isotherm sorption curves of type II of Brunauer`s classification (Mark D., 2001).

The mean relative percent deviation (%E) values were, in all cases, less than 5%, is an indication that the model is well suited for describing sorption isotherm of Aspirin(Menkov D. et al., 2004).

The Henderson Model

It is predicts greater changes in equilibrium moisture content for a given temperature change at high water activity. The model fits the lower part of the sorption isotherm curve (Ludger O. et al., 2003).

The Henderson model is:

$$1 - a_w = \exp\left[-a(x_w)^b\right] \qquad (9)$$

This may be written as follows:

$$\ln\left[-\ln\left(1 - a_w\right)\right] = b\ln x_w + \ln a \qquad (10)$$

By linear regression of eq. 10 using the experimental data, the constants of the model can be calculated. The results are shown in Tables 3 and 4, and Figs. 9, 10, and 11.

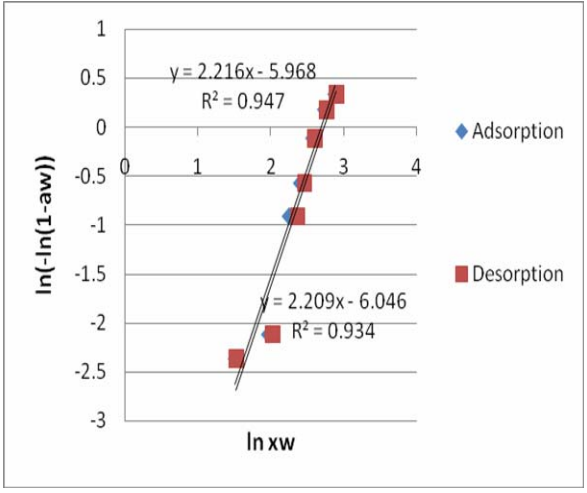

Fig. 9 Henderson model isotherm curves for Aspirin at 25 ºC

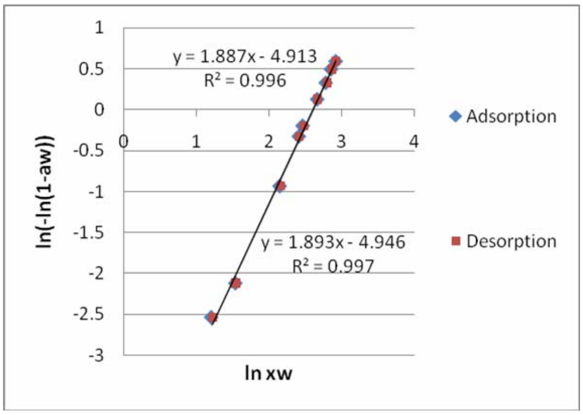

Fig. 10 Henderson model isotherm curves for Aspirin at 30 ºC

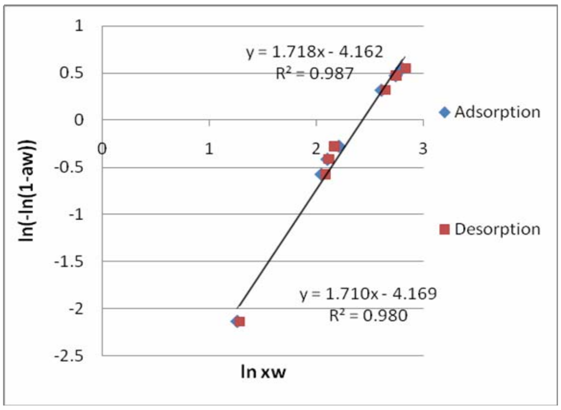

Fig. 11 Henderson model isotherm curves for Aspirin at 40 ºC

From the results, the regression coefficients were high and the mean percent relative deviation was lower than 5%.

Table 3: GAB and Henderson parameters of adsorption isotherms for Aspirin

Model	**Constants**	**25 ºC**	**30 ºC**	**40 ºC**
GAB	X_m	8.03	8.6	4.93
	C	49.5	12.06	11.46
	K	0.75	0.69	0.88
	R^2	0.973	0.995	0.972
	E%	4.1	3.32	3.14
Henderson	a	0.003	0.0075	0.0156
	b	2.218	1.887	1.718
	R^2	0.947	0.996	0.987
	E%	0.57	0.19	3.5

Table 4: GAB and Henderson parameters of desorption isotherms for Aspirin

Model	**Constants**	**25 ºC**	**30 ºC**	**40 ºC**
GAB	X_m	7.28	7.06	4.88
	C	58.25	26.6	9.72
	K	0.79	0.76	0.87
	R^2	0.962	0.952	0.972
	E%	0.84	4.04	4.3
Henderson	a	0.0024	0.007	0.0155
	b	2.21	1.893	1.71
	R^2	0.934	0.997	0.980
	E%	0.66	0.19	1.84

Comparing the results of the two models; the Henderson model fits the experimental data better than the GAB model.

CONCLUSIONS

The following conclusions are drawn from the above discussed results:-

1- The equilibrium moisture content increases with the water activity increase at any temperature, and decreases with an increase in temperature at constant water activity.

2- The water activity increases with increased temperature when moisture content was kept constant.

3- The sorption isotherm curves have an S-shape profile.

4- The monolayer moisture content and the sorption capacity decreased with an increase in temperature at constant water activity.

5- The hysterias effect was not distinctly expressed only for isotherms at 25 ºC.

6-The Henderson model is suitable for describing the sorption isotherms for Aspirin .

NOMENCLATURE

a_w	Water activity	(dimensionless)
a ,b	Constants of Henderson model	
c ,k	Characteristic constants of GAB model	
d .b.	Dry basis	
E	Mean relative deviation	(%)
ERH	Equilibrium relative humidity	(gH_2O/g dry solid)
P	Vapor pressure	(N/m^2)
P_0	Vapor pressure of pure water	(N/m^2)
R^2	Coefficient of regression	
X_w	Equilibrium moisture content	(%g H_2O /g dry solid)
$\hat{x}_w$	Predicted (calculated) moisture content	(%g H_2O /g dry solid)
X_m	GAB monolayer moisture content	(%g H_2O /g dry solid)
LOD	Loss on Drying	

Greek Letters

α, β, γ Constants of GAB model (in quadratic form).

REFRENCES

Acosta J., Nuevas L., Rodriguez I.," The Moisture Isotherms of Cefotaxime Sodium Salt", Drying Tech., V.18, 1-2, 2010.

Alexander G.," Water –Soluble Aspirin Composition", Patent 5776431, July, 1998.

Anthony J., Fontana Jr."Pharmaceutical Applications for Water Activity "Pharmaceutical on Line, April, 29, 1999.

Aroldo A. P., Abraham D.G. –Z., Fernando L. D.," Sorption Isotherms Experimental Data and Mathematical Models For Murici Pulp ", IDS, V. A , PP. 634-639 , 2004.

Bags K., Srivastav P. , Mishra H.," Desorption and Adsorption Characteristics of Bael Pulp and Powder ",International Food Research J.,16, PP.561-569,2009.

Bell L. N., Labuza T. P.," Practical Aspects of Moisture Sorption Isotherm and Use "2nd Edition AACC Egan Press., 2000.

Bob S. , Peihong L., Neil P.," Implementation of Water Activity Testing to Replace Karl Fischer Water Testing, " Pharmaceutical Tech. ,Feb., PP.56-71,2007.

Caurie M. A.," Practical Approach to Water Sorption Isotherms and the Basis for the Determination of Optimum Moisture Levels of Hydrated Foods ", J. Food Tech.., V.6, PP.85-93, 1970.

Charles R. Cunningham K.," The Effect of Starch on the Stability of Aspirin Tablets", American Association of Pharm. Scientists, Oct., 2004.

Cunningham C.," Formulations of Acetyl Salicylic Acid Tablets for Aqueous Enteric Film Coating", Pharm. Tech. Europe, May, 2001.

Daniel S. C., Wanderley P. O.,"Drying of Medicinal Plants : equilibrium Moisture Content and Mathematical Modeling of Maytenus Ilicifolia Leaves ", IDS , V.C,PP.1712-1719,2004.

Ethane C.S., Kahila M. , Lamharrer A.," Moisture Sorption Isotherms and Thermodynamic Properties of two Mints", Revue des Energies Renouvelables, V.11, No.2, PP. 181-195, 2008.

Greenspan L." Humidity Fixed Points of Saturated Aqueous Solutions", J. of Research of the National Bureau of Standards, V.81 A , No.1, pp.89-96, Jan-Feb, 1977.

Jhoany A. E., Vlisea J.H. and Galo C.R.," Behavior and Modeling of Humidity Isotherms of Mangifera Medical (Vimang) Powder ", J. World Applied Science, 11(12), PP.1504-1509, 2010.

Jiri B., Stavrosy Y."GAB Generalized Equation for Sorption Phenomena", Food Bioprocess Tech., No.1, PP. 82-90 , 2008.

Jorge C. , Ernsto O. Timmermann H. , A. Iglesias " Some Features of the Parameter k of the GAB Equation as Applied to Sorption Isotherms of Selected Materials ",J. of Food Engineering ,V.15 ,pp.75-82 ,1992.

Joseph A. , Simon V., Adesola S.," Moisture Adsorption Characteristic of Giner Slices ", Sienc. Technol. Aliment, 29(1), 155-164, Jan.-Mar., 2009.

Kim Huynh-Ba ,"Hand Book of Stability Testing in Pharmaceutical Development",Springer,2009.

Ludger O. F., Arther A. Teixeira "Food Physics: physical Properties –Measurement and Applications", Springer, 2003.

Maria L., Panagiotis G. D. ,"Equilibrium Moisture Characteristics of Food –Hysterias Effects and Isotherm Models ",Lebensmilel-Technologie ,26 ,No.4 ,1993.

Mark J. K., James J. C.," Water sorption of Drugs and Dosage Forms", Encyclopedia of pharmaceutical Tech., 2006.

Martin Chaplin, "Water structure and Science", 2009

Menkov D., Durakova G. ,"Moisture Sorption Isotherms of Walnut Flour at Several Temperatures",Biotechnol and Biotechnol.Eq.,2004.

Milton C., Afonso M., Paulo C.,"Drying Curves and Water Activity Evaluation of Dried Banana" , IDS, 22-25,Aug.,V.C,PP.2013-2020,2000.

Motta L. O. , Guilherme D. M., Roberta M.L.," Moisture Equilibrium Isotherms for A Handmade Kraft Paper ", IDS, V.B, PP.1241-1248, 2004.

Motta L. O., Carlos E.S., Nehemias C.," Moisture Equilibrium Isotherms for Pinnus Long Fiber Cellulose", Acta Scientiurum Tech., No.1,V.26, PP.27-32,2004.

Rahman m. s., Shyams S.S., Labuza T.P.," Measurement of Water Activity Using Isopiestic Method, "Current Protocols in Food Analytical Chemistry, 2000 Rouquerol F., Rouquerrol J., Sing K.," Adsorption by Powders and Porous Solids", Academic Press , London ,1999.

Susan K., Donald C. P.," Aspirin", http://elephant cares org., 2003

Shyam S. S., Rahman P. L. ,Theodol P. L.," Measurement of Water Activity using Isopiestic Method ", Food Analytical Chemistry ,A 2.3.1.-A 2.3.10,2001.

Thommes M., Kohn R., Froba M.," Sorption and Pore Condensation Behavior of Pure Fluids", Appl. Surface Sci. 196, PP.239-249, 2002.

Sumie Y.,Valeatimo J.," Stability of Drugs and Dosages Forms",2008.

Wolf W. , Spiess W. E., Jung G.," Standardization of Isotherm Measurement", (COST-90 and 90 BIS), Properties of Water in Foods, PP.661-678 , 1985.

Yanxia L., Yeshwaut D., Sanzgiri Y.C.,"A Study on Moisture Sorption Isotherms of Formulations" , AAPS Pharm. Sci. Tech. , 4(4), 59, 2003.

Yihong Q., Yisheng C., Liroug L.,Geoff G.," Developing Solid Oral Dosage Form: Pharmaceutical Theory and Practice ,Academic Press.,2009.