Available online at www.ijpab.com

DOI: http://dx.doi.org/10.18782/2320-7051.2364

ISSN: 2320 – 7051

Int. J. Pure App. Biosci. **4 (4):** 1-7 (2016)

Research Article

International Journal of Pure & Applied Bioscience

OPEN ACCESS

Validation of A Commercial Hand-Held Human Electronic Glucose Meter for use in Pigs

Rosa Elena Pérez Sanchez[1], Gerardo Ordaz Ochoa[2], Aureliano Juárez Caratachea[2]*, Rafael Maria Román Bravo[3], Ruy Ortiz Rodriguez[4]

[1]Facultad de Agrobiología "Presidente Juárez"- Universidad Michoacana de San Nicolás de Hidalgo. Paseo Lázaro Cárdenas-Berlín Col. Viveros. Uruapan Michoacán, México

[2]Instituto de Investigaciones agropecuarias y Forestales-Universidad Michoacana de San Nicolás de Hidalgo. Km 9,5 Carretera Morelia-Zinapécuaro. Tarímbaro Michoacán, México. CP 58880

[3]Facultad de Ciencias Veterinarias. Universidad del Zulia. Maracaibo, Venezuela.

[4]Facultad de Medicina Veterinaria y Zootecnia-Universidad Michoacana de San Nicolás de Hidalgo. Km 9,5 Carretera Morelia-Zinapécuaro. Tarímbaro Michoacán, México. CP 58880

*Corresponding Author E-mail: aurelianojuarez@hotmail.com

Received: 22.08.2016 | Revised: 27.08.2016 | Accepted: 30.08.2016

ABSTRACT

The objective of this work was to validate the analytical accuracy of an Accu-Chek Performa® glucometer to determine blood glucose in pigs, taking as reference the conventional laboratory (CM) method. It was used forty preprandial blood samples taken from sows (two samples/sow) with a live weight of 89.1±5.6 kg. The concordance degree between both methods was carried out by using Bland-Altman graphic procedures and estimation of Lin's concordance correlation coefficient (CCC), and by using the established recommendations from the Clinical and Laboratory Standards Institute (CLSI). Glycemic averages were 77.1 and 76.4 mg/dL, with 95% confidence intervals between 71.5 and 82.9 mg/dL and 70.2 and 82.5 mg/dL for the glucometer method (GM) and CM, respectively. Both methods showed a linear relationship: r=0.99 and R^2=0.97 (P<0.05). According to CLSI, glycemic results found using GM were considered as acceptable; results confirmed by the Bland-Altman analysis and Lin's CCC (0.95; P<0.05). Hence, the hand-held human glucometer is a viable device for monitoring glucose in pigs not only by its accuracy, but also because it reduces both stress and costs during sampling in comparison to CM.

Key words: *Glycemic, association, concordance, linearity, correlation.*

INTRODUCTION

Glucose is the main molecule involved in the direct energy input to carry out physiological processes[1]. Hence, maintaining adequate monosaccharide body levels is essential for regulating energetic metabolism and for maintaining homeostasis[2].

Cite this article: Sanchez, R.E.P., Ochoa, G.O., Caratachea, A.J., Bravo, R.M.R. and Rodriguez, R.O., Validation of A Commercial Hand-Held Human Electronic Glucose Meter for use in Pigs, *Int. J. Pure App. Biosci.* **4(4):** 1-7 (2016). doi: http://dx.doi.org/10.18782/2320-7051.2364

Currently, people's lifestyle changes also has brought glucose patterns changes, making it one of the most common metabolic pathologies[3,4], and therefore blood glucose monitoring has become an everyday event[5].

Similarity to humans in pigs (and other animals) it is required blood glucose levels changes evaluation in each physiological or pathologic stage in which they are[6] to link these glucose levels with health or productivity of these species[7]. Thus, for example, blood glucose is directly related to feed intake[8], fetus' development[9]; milk quality[10]; weight gain[11], among other variables. For these reasons, it is fundamental monitoring glucose levels in pigs and, thus through these levels allowing farmers to control and to manipulate biological events inherent to this specie productivity[12].

In general, blood glucose determination in farm animals under field conditions is difficult, mainly because of particular procedures related to its analysis such as animal restraining, sampling, analysis cost and stress caused[13]. In comparison with the process to determine blood glucose in humans, which is through a hand-held electronic glucometer with the following benefits: speed; minimum sample volume (0.6 µL) reduces both time and financial investment for getting results[14,15]. In addition, the procedure to determine glucose with an electronic glucometer avoids effects of temperature, humidity or sample volume on the blood glucose measurement[3]. Such benefits would reduce the inconveniences in the determination of glucose in pigs, in addition observing procedures associated to animal welfare guidelines[13].

Therefore, the hand-held electronic glucometer developed for human use can be an alternative in blood glucose measurements in farm animals, particularly pigs, because this specie has physiological similarities with humans. For this reason, the objective of this work was to validate analytical accuracy of an electronic glucometer (Accu-Chek Performa®) with glucose measurements in pigs, considering as a control method of blood glucose measurement a standard kit Clonatest Glucose MR® in laboratory conditions.

MATERIAL AND METHODS

Animals and housing

Twenty hybrid sows (York x Landrace x Pietrain) with a liveweight of 89.1±5.6 kg randomly selected from the productive herd. Five days before blood sampling, the sows were located in two groups of 10 animal in pens of 12 m^2 equipped with automatic stainless steel hopper feeder, model IPASA CE181IF® with dimensions of 78 cm long, 70 cm wide and 121 cm high which equals a capacity of 160 kg capacity to feed 50 pigs. Water supply was using an automatic type drinker nipple; both, food and water were supplied *at libitum* strategy.

Sampling and glucose determination

After 8 hours fasting, two paired blood samples were taken at 8:00 a.m. (two per sow, n=40) to establish the differences between the evaluation methods. In order to determine blood glucose through the conventional laboratory method (CM), 5 ml of blood (n=20) was extracted from the jugular vein with a 5 ml syringe capacity with a 20G and 2.0 inches hypodermic needle, once extracted, blood samples were stored in tubes BD Vacutainer® provided whith clot activator. Each sample was stored at 4° C until analysis 4 h after collection. The CM glucose determination requires removing the clot, centrifuging the supernatant at 3500 rpm for 10 minutes to obtain serum samples, and then processed according to manufacturer instructions.

The kit of blood glucose determination is an enzymatic colorimetric method based on the reaction of Trinder1, 2; glucose is oxidized by glucose oxidase (GOD) to D-gluconate with formation of hydrogen peroxide. In the presence of peroxidase (POD), phenol and 4-aminoantipyrine (4-AA) is condensed by the action of hydrogen peroxide forming a quinoneimine network proportional to the glucose concentration in the sample[16].

In relation to the electronic glucometer method (GM), it was required 0.6 µL blood samples per sow (n=20), which was taken

from the posterior auricular vein. The evaluation of blood glucose by GM was immediately after depositing the sample in the GM test strip. The GM uses a principle of electrochemical analysis, so, this method provides a high level of sensitivity and accuracy.

Statistical analysis

The results obtained by the CM and GM methods were analyzed using the statistical criteria of the Clinical and Laboratory Standards Institute[17] same it based on paired "t" test. First, It was performed a Kolmogorov-Smirnov test. Second, the outliers were identified comparing the absolute differences between each method; these differences must not exceed four times the value of the mean of the absolute differences. Third, if the correlation coefficient (r) was greater than or equal to 0.975, the range of values were considered as adequate and, therefore, linear regression parameter estimation can be performed. Fourth, it was estimated the slope and intercept for the data values, as well as, their respective 95% confidence intervals (CI). Finally, it was tested the systematic estimation error and CI in each method, according to levels of clinical decision for blood glucose, from the fitted linear regression equation.

Once met the five criteria, the concordance between both methods was assessed (CM *vs* GM) by Bland-Altman's graphical analysis, and Lin's concordance correlation coefficient determination (CCC). For these analyzes SAS statistical package was used[18].

RESULTS AND DISCUSSION

The paired "t" test for the difference between glucose levels for the two determination methods was not statistically significant ($P > 0.05$). The glucose average values were 77.1 *versus* 76.4 mg/dL for GM and CM, respectively. The CI for the GM was between 71.5 and 82.9 mg/dL, whereas it was between 70.2 and 82.5 mg/dL for the CM. On the other hand, the coefficient of variation (CV) for the difference between both methods was only 1.6%. (Table 1). With regard to the differences between the glucose values obtained by both methods, these were 2.5 mg /dL for the minimum values, 1.0 mg/dL for the maximum values and 0.7 mg/dL for the arithmetic mean. In this aspect, the CLIA[17] establishes that, for glycemic quality specifications, values obtained by alternative methods, must not exceed 10% of variability relative to values reported by the conventional method or 5.4 mg/dL, which agrees with the value found in this validation work. Therefore, the analyzed GM (Table 1) satisfies the quality standard stipulated by the CLIA.

In order to establish the feasibility of the validation of the GM to be used as an alternative in glycemic determination in pigs, the value of the CV differences found between both methods (1.6%; Table 1) was considered as acceptable. Since the maximum accepted CV value is 5% to validate a reliable alternative method[18]. In addition, the variation found (1.6%) between both methods was lower than that suggested by various international agencies to declare a method as reliable (Table 2).

Table 1: Descriptive glycemia results obtained by glucose meter (Accu-Chek Performa®) and conventional method of laboratory (Glucose Clonatest MR®)

	METHOD	
Values	Clonatest Glucose MR®	Accu-Chek Performa®
Values of glycemia minimum, mg/dL	54.9	57.4
Values of glycemia maximum, mg/dL	104.0	105.0
Arithmetic mean, mg/dL	76.4	77.1
	CI (70.2 a 82.5)	CI (71.5 a 82.9)
Coefficient of variation		
Maximum, %	0	
Minimum, %	6.0	
Mean, %	1.6	

CI = confidence intervals 95%.

Poirier *et al.*[20] classified methods as reliable and acceptable or unacceptable based on the variation contrasted with conventional methods. Thus, a glucometer is reliable when 60% of the results are within the range ±10%[20]. In this sense, an electronic glucometer for human use can be considered as a reliable method for glycemic levels determination in pigs (Table 2).

Table 2: Quality specifications for glycemia according to various international standards

International organization	Quality criteria
ADA	100% values ± 5% compared to the reference method.
ISO 15197	95% values ± 15% for values ≤ 75 mg/dL
	100% values ± 20% for values ≥ 75 mg/dL
CLIA	Values obtained ± 10% o 5.4 mg/dL regarding values usual method.

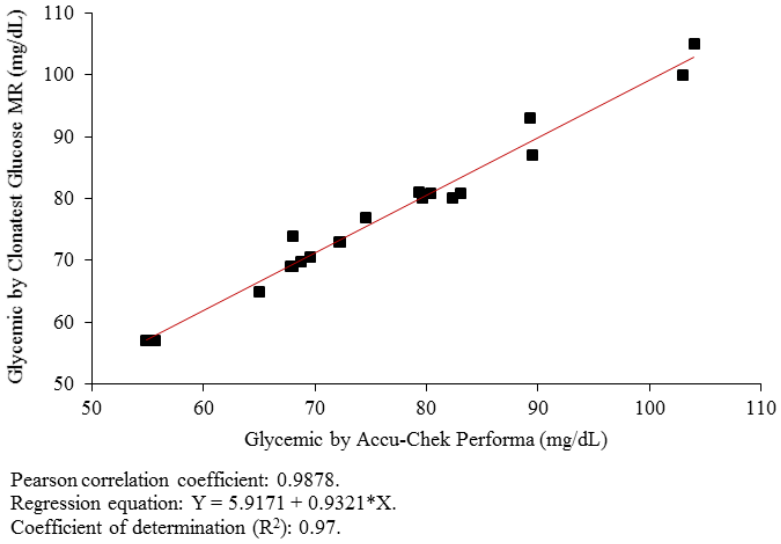
ADA: American Diabetes Association; ISO: International Organization for Standardization; CLIA: Clinical Laboratory Improvement Amendments.

The results of the Kolmogorov-Smirnov test showed that, glycemic serum values obtained by GM and MC observed a normal distribution with probabilities of 0.177 and 0.121 for CM and GM, respectively, without finding values higher than one standard deviation. In addition, the Pearson correlation coefficient (r) was 0.99 ($P<0.05$) with a determination coefficient of 0.97, thus, indicating a strong linear association. This suggested that the analytical method maintained the ratio between the true glucose concentration and the response[21].

It has been established[22] that, for a calibration curve, Pearson's correlation must be equal or greater than 0.99, although, in the case of traces is supported a value equal to 0.99. However, there are controversies about the implementation of the correlation coefficient to determine linearity in the validation of a method[21,22]. In this situation, Morón *et al.*[21] indicated that the best indicator to establish the linearity in the validation of an analytical method, in replacement of Pearson's correlation coefficient is computing the probability at which it is statistically significant by using a Student 't' test (tr) with n-2 degrees of freedom. In this regard, results of this research showed that *tr* was significant ($P = 0.05$).

In contrast to the *tr* method the Lin's concordance correlation coefficient (CCC), qualifies the association strengths as, almost perfect, considering values greater than 0.99; substantial, from 0.95 to 0.99; moderate, 0.90 to 0.94 and poor, below 0.90[23,24]. In this research, the Lin's CCC was 0.9501 with CI 95% from 0.9487 to 0.9532; which, suggest that glucose levels determinations in pigs obtained by GM is within the category of substantial concordance. Therefore, the implementation of the glucometer as alternative method in glycemic measurements in pigs can be considerable as viable considering the results already pointed out by this work (r, R^2, *tr* and CCC).

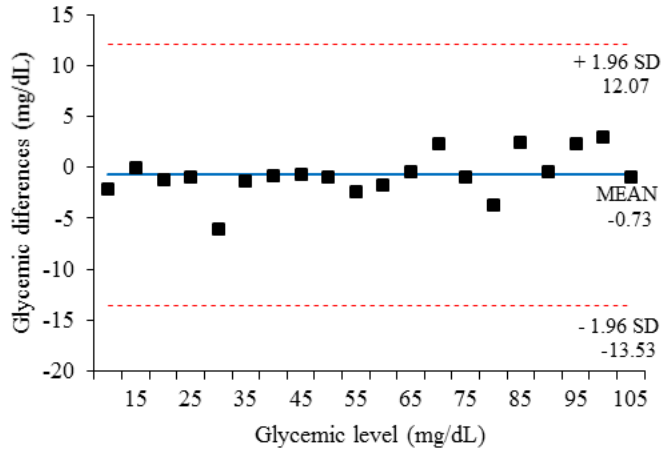
Once fulfilled these criteria (r, R^2, *tr* or CCC), it is necessary to use a linear regression equation to check the linearity of the measurement techniques that are assessed by evaluating how close are the observed points in comparison to the estimated straight line[21]. In this respect, the values of the linear equation coefficients were for the intercept 5.9171 and for the slope 0.9321, both significant values ($P < 0.05$) by plotting the predicted and the observed values it suggests a strong relationship (Figure 1).



Pearson correlation coefficient: 0.9878.
Regression equation: Y = 5.9171 + 0.9321*X.
Coefficient of determination (R^2): 0.97.

Fig. 1: Linear Estimation between conventional method (CM) of laboratory and glucose meter (GM)

The concordance presented by statistical analyzes described above was also assessed by the Bland-Altman graphic method (Figure 2); in order to assess whether or not the differences between values found showed any relevance from the clinical point of view[3]. Results for the application of the Bland-Altman graphic method showed a systematic bias of -0.73 mg/dL, and a limit of concordance between -13.53 and 12.07 mg/dL; values outside the limits that make the difference greater than ±1.96 standard deviation were not found .



SD= standar desviation

Fig. 2: Bland-Altman Graphic among of conventional method (CM) of laboratory and glucose meter (GM)

The difference between CM and GM was constant at all glycemic levels, this according to Bland-Altman analysis (Figure 2). The minimum difference ($P > 0.05$) observed between CM and GM were probably because glucometer strips, were calibrated for whole blood glucose determination; while in the conventional laboratory method was used serum samples, which may show variation ≤15%, which can be considered as acceptable[20,24].

CONCLUSIONS

The electronic glucometer for human use (Accu-Chek Performa®) is a suitable method

to monitor pigs' glycemic levels not only for its accuracy but also because glucose determinations are carried out easily in this specie, it reduces both stress and sampling cost due to process, compared to conventional laboratory methods.

Acknowledgements

We want to thank the UMSNH Facultad de Medicina Veterinaria y Zootecnia and CONACYT the former for the support and the later for funding awarded for this research.

REFERENCES

1. Castrejón, V., Carbó, R., & Martínez, M. Mecanismos moleculares que intervienen en el transporte de glucosa. *Revista de Educación Bioquímica,* **26(2):** 49-57 (2007).
2. Rao, D.T., Sunio, L.K., Lo, Y.J., & Gossain, V.V. Comparison of the Adherence to the American Diabetes Association Guidelines of Diabetes Care in Primary Care and Subspecialty Clinics**.** *Journal of Diabetes and Metabolism Disorders,* **24:** 14-35 (2015).
3. Castaño, M., Fernández, J., Robles, J., & Márquez, T. Validation of glucose meter at an intensive care unit. *Endocrinología y Nutricion,* **59(1):** 28-34 (2012).
4. Alhabashneh, R., Khader, Y., Herra, Z., & Assad, F. The association between periodontal disease and metabolic syndrome among outpatients with diabetes in Jordan**.** *Journal of Diabetes and Metabolism Disorders, **14:** 76* (2015).
5. Quispe, F.A.L. Prevalencia de diabetes mellitus en la I campaña de detección precoz de diabetes en la población adulta de Huarina. Revista Médica La Paz, **15(1):** 41-46 (2009).
6. Park, M.S., Yang, Y.X., Shinde, P.L., Choi, J.Y., Jo, J.K., Kim, J.S., Lohakare, J.D., Yang, B.K., Lee, J.K., Kwon, I.K., & Chae, B.J. Effects of dietary glucose inclusion on reproductive performance, milk compositions and blood profiles in lactating sows. *Journal of Animal Physiology and Animal Nutrition,* **94(5):** 677-684 (2010).
7. Almaguel, G.R.E., Ly, J., & Cruz, M.E. Índices bioquímicos en sangre de cerdos alimentados con mieles intermedias de caña de azúcar y una dieta de cereales. *Revista Electrónica de Veterinaria,* **13(6):** 1-8 (2012).
8. Pére, M.C., & Etienne, M. Insulin sensitivity during pregnancy, lactation, and postweaning in primiparous gilts. *Journal of Animal Science,* **85(1):** 101-10 (2007).
9. Kemp, B., Soede, N.M., Vesseur, P.C., Helmond, F.A., Spoorenberg, J.H., & Frankena, K. Glucose tolerance of pregnant sows is related to postnatal pig mortality. *Journal of Animal Science,* **74(4):** 879-885 (1996).
10. Hansen, A.V., Strathe, A.B., Kebreab, E., France, J., & Theil, P.K. Predicting milk yield and composition in lactating sows: A Bayesian approach. *Journal of Animal Science,* **90:** 2285–2298 (2012).
11. Van Der Peet-Schwering, C.M.C., Kemp, B., Binnendijk, G.P., Den Hartog, L.A., Spoolder, H.A.M., & Verstegen, M.W. Performance of sows fed high levels of nonstarch polysaccharides during gestation and lactation over three parities. *Journal of Animal Science,* **81:** 2247-2258 (2003).
12. Cools, A., Maesb, D., Decaluwéa, R., Buysec, J., Kempend, T. A., Liesegange, A., & Janssens, G.P. Ad libitum feeding during the peripartal period affects body condition, reproduction results and metabolism of sows. *Animal Feed Science and Technology,* **145:** 130–140 (2014).
13. Liljenstolpe, C. Evaluating animal welfare with choice experiments: an application to Swedish pig production. *Agribusiness,* **24:** 67–84 (2008).
14. Thompson, M., Ellison, S.L.R., & Wood, R. Directrices armonizadas para la validación de métodos de análisis por un solo laboratorio. *Pure and Applied Chemistry,* **74(5):** 835-855 (2002).
15. Saldaña, O.M.I. Reliability of a gas analyzer to determine glycemia compared to the conventional laboratory method.

Anales de la Facultad de Medicina, **75(3):** 227-232 (2014).

16. Khan, A.I., Vasquez, Y., Gray, J., Wians, F.H.Jr., & Kroll, M. H. The Variability of Results between Point-of-Care Testing Glucose Meters and the Central Laboratory Analyzer. *Archives of Pathology & Laboratory Medicine, 130,* 1527-32 (2006).
17. CLIA: Requeriments for Analytical Quality. The Poor Lab's Guide to the Regulations. Retrieved from https://www.westgard.com/clia.htm
18. SAS: Statistical Analysis System Institute. Guide for personal computers. Version 8. (2010).
19. Skeie, S., Thue, G., & Sandberg, S. Patient-derived quality specification for instruments used in self-monitoring of blood glucose. *Clinical Chemistry* **47:** 67-73 (2001).
20. Poirier, J.Y., Le Prieur, N., Campion, L., Guilhem, L., Allannic, H., & Maugendre, D. Clinical and statistical evaluation of self-monitoring blood glucose meters. *Diabetes Care*, **21:** 1919-1924 (1998).
21. Morón, C., Zacarías, I., & dePablo, S. Producción y manejo de datos de composición química de alimentos en nutrición. *Instituto de nutrición y tecnología de los alimentos. FAO Universidad de Chile* (2007).
22. Duffau, B., Rojas, F., Guerrero, I., Roa, L., Rodríguez, L., Soto, M., Aguilera, M., & Sandoval, S. Validación de métodos y determinación de la incertidumbre de la medición: "Aspectos generales sobre la validación de métodos". *Guía técnica. Instituto de salud pública Chile.* **1:** 21-49 (2010).
23. Camacho, J. Coeficiente de concordancia para variables continúas. *Acta Médica Costarricense*, **50(4):** 211-212 (2008).
24. Karon, B.S., Griesmann, L., Scott, R., Bryant, S.C., Dubois, J.A., & Shirey, T.L. Evaluation of the impact of hematocrit and other interference on the accuracy of hospital-based glucose meter. *Diabetes Thecnology*, **10:** 111-120 (2008).