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CURRENT BREAKTHROUGHS IN REAL-TIME GLUCOSE TRACKING DEVICES FOR DIABETES

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Abstract

The pharmaceutical industry is undergoing a significant transformation driven by the integration of digital technologies, collectively known as Industry 4.0. This shift is redefining how drugs are developed, manufactured, and distributed. Key technologies such as the Internet of Things (IoT), Artificial Intelligence (AI), and big data analytics are at the forefront of this change, enabling smart manufacturing, real-time process optimization, and enhanced supply chain management. IoT facilitates the creation of interconnected production environments where sensors and devices continuously monitor critical parameters, ensuring optimal conditions and predictive maintenance. AI accelerates drug discovery through predictive modeling, automates quality control processes, and employs predictive analytics to enhance maintenance and process improvement. Big data empowers data-driven decision-making, ensures regulatory compliance through comprehensive analysis, and supports the shift toward personalized medicine by enabling customized drug production. Despite the significant benefits, the adoption of these technologies poses challenges, including integration with existing systems, data security concerns, and navigating a complex regulatory landscape. This review explores these technologies' impact on pharmaceutical manufacturing, highlighting successful case studies and best practices. Additionally, it discusses the future directions, including the move towards fully autonomous systems and the importance of collaboration between tech companies, manufacturers, and regulators to drive innovation and ensure compliance. The continued evolution of digital technologies in pharma manufacturing promises to enhance efficiency, reduce costs, and deliver more personalized treatments.

Keywords: CGM, Sensors, Technology, Glucose, Wearable, Dexcom.

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Introduction

Continuous glucose monitoring (CGM) systems rely on glucose oxidation reactions to track blood glucose levels. Diabetes, a chronic metabolic disorder, requires 24/7 management through diet, exercise, and medication/insulin therapy. Accurate blood glucose measurement is crucial for effective management. Self-monitoring blood glucose (SMBG) meters, introduced in the late 1970s, enabled individuals to track their glucose levels at home. However, SMBG has limitations, and CGM systems have emerged as a more comprehensive solution. CGM sensors must meet specific requirements, including biocompatibility, lifetime, safety, sensitivity, and specificity. The glucose oxidation reaction is the most popular technique used in CGM systems. Diabetes management relies heavily on accurate glucose measurement, and CGM systems provide a more detailed picture of glucose levels throughout the day. Effective diabetes management requires careful monitoring and adjustment of treatment plants [1]. Continuous Glucose Monitoring (CGM) technology has revolutionized diabetes management over the past decade. CGM devices provide on-demand glucose information, including current readings, trends, and patterns. This data helps healthcare professionals and individuals with diabetes make informed decisions about treatment. CGM devices can be transcutaneous or implantable, transmitting glucose readings wirelessly to a reader or smartphone app. Some devices, like the FreeStyle Libre system, use intermittently scanned CGM (is CGM) or FLASH glucose monitoring, transmitting data only when scanned. The accuracy of CGM devices has been well validated compared to reference plasma glucose measurements. CGM technology enables users to track their glucose levels in real-time, identify patterns and trends, and adjust their treatment plans accordingly. This has improved diabetes care and management, allowing individuals to take a more active role in their health [2]

History of CGM sensors

The development of Continuous Glucose Monitoring (CGM) devices has undergone significant advancements since the first professional CGM system was approved by the FDA in 1999. Early systems, such as the Medtronic Real-Time Guardian, had limitations, including poor accuracy, with a Mean Absolute Relative Difference (MARD) of 15%. However, subsequent generations of CGM devices have improved accuracy and functionality [3]. The Dexcom SEVEN Plus, for example, had a MARD of 16.7% and lasted up to 7 days. Newer devices, such as the Medtronic Enlite CGM system and Abbott's Freestyle Navigator II, have achieved even better accuracy, with MARD values of 13.6% and 12.3%, respectively. These advancements have enabled CGM devices to become more comfortable, user-friendly, and reliable, providing individuals with diabetes with more accurate and actionable data to manage their condition [4].

Wearables for glucose biosensing

Wearable sensing devices, including Continuous Glucose Monitoring (CGM) systems, offer attractive opportunities for disease prediction, diagnosis, and prevention. CGM devices provide real-time blood glucose levels, relying on precise and accurate biosensors. Biosensors consist of a bioreceptor, signal transducer, and signal displayer, detecting biological analytes and relaying their concentrations. There are various classes of biosensors, including catalytic and affinity biosensors. Non-enzymatic biosensors and aptamers show promise as recognition molecules for glucose detection [5]. Glucose levels in sweat, saliva, urine, tears, and interstitial fluid can be correlated to blood glucose levels. Wearable biosensing devices monitoring glucose in these fluids demonstrate potential as non-invasive, pain-free alternatives to finger-pricking methods. Designing wearables for monitoring glucose in different body fluids requires distinct approaches. These advancements aim to improve the quality of life for millions of people with diabetes [6].

CGM sensor technologies

In recent years, various glucose-sensing mechanisms for non-invasive, or at least minimally invasive, CGM have been tested, in an attempt to match all fundamental requirements for an extended in vivo use, e.g., sensitivity, specificity, linearity within biological relevant range, biocompatibility, and lifetime [7]. Measures an electrical current signal generated by the glucose-oxidase reaction. This signal is proportional to the glucose concentration available in the interstitial fluid, which is then converted into a glucose concentration by a calibration procedure usually performed twice a day. The devices based on this principle employ a minimally-invasive needle sensor, usually inserted in the subcutaneous tissue, in the abdomen or on the arm.

(c) (d)

Figure: 1 (a) A Patient Wearing a Sensor; (b) Medtronic Elite Sensor with Dedicated Inserter Device; (c) Dexcom G5 Mobile with Share Technology; (d) Abbott Freestyle Navigator.

The early age of glucose-oxidase CGM sensors

The development of glucose-oxidase based Continuous Glucose Monitoring (CGM) sensors began in the late 1990s. Initial prototypes faced biocompatibility issues, but commercial systems emerged in 2005, including Medtronic Guardian, Dexcom Seven Plus, and Abbott Navigator. Accuracy was assessed using Mean Absolute Relative Difference (MARD), with values ranging from 12.8% to 16.7%. Although CGM sensors have improved, their accuracy still lags behind Self-Monitoring Blood Glucose (SMBG) systems. CGM manufacturers have prioritized developing more accurate sensor systems over the past decade, as accuracy is crucial for informing critical therapeutic decisions, such as insulin dosing. Further improvement is needed.

State-of-art glucose-oxidase sensors

Medtronic's Enlite sensor, launched in 2011, offered improved accuracy and comfort. The sensor's design was revamped to reduce inflammatory responses, and its size was decreased. The wear time was extended to six days, and the inserter device became more user-friendly. These changes improved usability and accuracy, achieving a 13.6% MARD[8]. Dexcom's G4 Platinum sensor, introduced in 2014, further enhanced accuracy with a 9% MARD. The G4 Platinum sensor was also equipped with Share technology, allowing secure wireless connections to smartphones and designated recipients. Dexcom's G5 Mobile CGM system, launched in 2015, enabled direct wireless communication to smartphones without a dedicated receiver. Abbott's FreeStyle Navigator II CGM system, launched in 2011, featured a redesigned receiver, smaller transmitter, and improved sensor design, reducing warm-up time from 10 to 1 hour. These advancements have improved the accuracy, usability, and connectivity of CGM systems [9].

Clinical impact of CGM sensors

Advanced Continuous Glucose Monitoring (CGM) systems have improved diabetes management, reducing HbA1c levels and hypoglycemic episodes. Next-generation CGMs aim to enhance accuracy, reliability, and usability through hardware and software advancements. These improvements will increase patient and clinician confidence, ultimately leading to better diabetes care and management outcomes over time [10].

Technological trends and challenges for the next generation of CGM sensors

The development of next-generation Continuous Glucose Monitoring (CGM) systems focuses on smaller, longer-lasting devices. Companies like Dexcom and Google are working together to create smaller, cheaper, and longer-lasting CGM products. The Eversense sensor, a fully implanted CGM, offers real-time glucose measurements for up to 90 days with an accuracy of 11.4% MARD. Its lifetime and ease of use are significant advantages. Beyond hardware improvements, next-generation CGM systems must also address software requirements, such as data management, integration with external devices, and smart features like alerts and alarms for hypoglycemic or hyperglycemic events. Incorporating glucose trend information and detecting sensor faults are also essential. Future CGM systems will need to balance hardware and software advancements to provide users with more convenient, accurate, and connected glucose monitoring experiences. This will enable better diabetes management and improved patient outcomes[11].

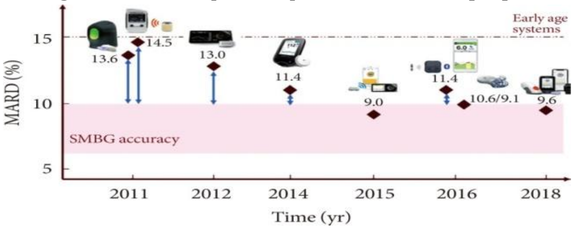

Figure 2 Accuracy evolution of state-of-art CGM systems through years.

Next-generation Continuous Glucose Monitoring (CGM) systems are exploring new glucose sensing technologies beyond glucose-oxidase. Fully implanted sensors, like the Eversense CGM, offer longer lifetimes but require surgical procedures. Data security is also crucial, as CGM transmitters have security weaknesses that make user data vulnerable to hacking. The Diabetes Technology Society has established DTSec, a standard for ensuring high security and assurance levels among diabetes treatment devices, including CGM systems. Future CGM products are expected to be more accurate, smaller, and user-friendly, with improved data management and smart features [12].

The role of CGM in decision support tools

Type 1 diabetes (T1D) therapy involves multiple daily insulin injections to maintain blood glucose levels within a safe range. This approach is demanding, requiring frequent blood glucose monitoring, insulin injections, and adjustments based on diet and physical activity, resulting in over 500,000 actions in a lifetime.

Bolus calculator

A first simple tool devised to provide decision support to T1D patients is the so-called bolus calculator a software that implements a simple formula for computing the amount of insulin to inject subcutaneously which is expected to compensate for carbohydrates intakes. The formula for calculating the recommended dose of insulin, B (U) is:

$$B = CHO/CR + GC - GT /CF - IOB, \quad (1)$$

where the carbohydrate-to-insulin ratio (CR) (g/U), which specifies the number of grams of carbohydrate covered by each unit of insulin, and the correction factor (CF) (mg/Dl /U),which represents the drop in BG level caused by each unit of insulin, are two patient specific parameters usually tuned up by physician with empirical laws and trial-and-error procedures [13], CHO (g) is the estimated amount of carbohydrates in the meal, GC (mg/dL) is the current BG level, GT (mg/dL) is the target BG level and IOB (U) is an estimate of the amount of insulin previously injected in the body not been assimilated yet. Bolus calculators have improved blood glucose control and quality of life for diabetes patients by reducing hypo/hyperglycemic events. However, their effectiveness is limited by patients' ability to accurately estimate carbohydrate intake, as small errors can significantly impact postprandial glycemia. Additionally, the calculator's parameters, such as carbohydrate-to-insulin ratio and correction factor, can vary throughout the day due to physiological factors. Furthermore, the formula does not utilize dynamic information from Continuous Glucose Monitoring sensors, such as trend data, which could enhance its accuracy and effectiveness in diabetes management. These limitations highlight areas for improvement [14].

Technological solutions to improve bolus calculators

Researchers are developing tools to automatically assess carbohydrate content in a patient's diet, addressing a weakness in current bolus calculators. Mobile apps, utilizing phone features like cameras and microphones, are being developed to estimate carbohydrate content. For example, GoCARB is an Android app that uses computer vision techniques to estimate nutritional content from photos of meals. A pilot study showed encouraging results in 20 adults with Type 1 diabetes. Another approach is the VoiceDiab expert system, which combines a nutrient database with automatic speech recognition. Patients describe their meal vocally and receive recommended insulin doses [15]. A crossover randomized controlled study in 12 Type 1 diabetes adults showed promising results. These innovative solutions aim to improve carbohydrate estimation accuracy, enhancing diabetes management and patient outcomes. By leveraging mobile technology, these apps have the potential to simplify and improve the accuracy of carbohydrate tracking.

Use of CGM information to improve bolus calculators

A dynamic approach to bolus calculation adjusts carbohydrate-to-insulin ratio (CR) and correction factor (CF) using Continuous Glucose Monitoring (CGM) data. This method employs a run-to-run control technique, updating CR and CF daily based on performance metrics, such as postprandial glucose levels. Simulation studies involving 10 adults and 10 adolescents demonstrated the effectiveness of this approach in adapting to individual patient needs[16]. Studies have shown that a dynamic approach to bolus calculation, using run-to-run (R2R) control and case-based reasoning (CBR), can significantly improve glycemic metrics and reduce time spent outside the safety range. However, these methods rely on a single blood glucose measurement, which may not provide a complete picture of the patient's status. To improve outcomes, researchers have proposed modulating the recommended insulin dosage based on the patient's current rate of change (ROC) in glucose levels. This can be achieved by empirically adjusting the current glucose level according to ROC or by modulating the whole meal dose by a fixed percentage. By incorporating ROC into bolus calculation, aim to create more effective and personalized treatment plans for patients with diabetes. This approach has the potential to improve glycemic control and reduce the risk of complications [17].

Figure 3. Example of Implantable CGM System Based on optical sensing technique, the Senseonics eversense continuous glucose monitoring system.

Advanced application based on real time CGM

The increased amount of available information brought by wearable devices, such as CGM systems and physical activity monitoring bands, has led to the development of decision-making tools and applications that can enhance the manage¬ment of the disease [18]. A Decision Support System (DSS) provides personalized and proactive support for individuals with diabetes, enabling quicker reactions to changing conditions. This technology has gained traction in healthcare, allowing for automatic data collection, transmission, and analysis. By integrating e-health and tele-monitoring systems, DSSs can improve glycemic outcomes for Type 1 Diabetes Mellitus (T1DM) patients by preventing hypo- and hyperglycemic events and reducing uncertainty in self-management decisions. This can lead to better diabetes management and improved patient outcomes[19]. Since 2006, integrated medical devices combining Continuous Glucose Monitoring (CGM) sensors and insulin pumps have been available. The Medtronic MiniMed Paradigm REAL-time system was the first, followed by the Paradigm Veo and MiniMed 530G, which featured low glucose suspend (LGS) to automatically stop basal insulin infusion when CGM readings fell below a set threshold. Newer Medtronic systems, such as the MiniMed 640G and 630G, include the SmartGuard feature, which predicts and prevents low glucose events by suspending basal insulin infusion when CGM readings are expected to drop below a preset threshold within 30 minutes [20].

Challenges and future perspectives

Diabetes is a chronic condition characterized by the body's inability to produce or effectively use insulin. As one of the four major noncommunicable diseases, diabetes poses a significant global health burden, with 85% of diabetes-related deaths occurring in developing countries due to limited access to testing and monitoring equipment. To address this, researchers have been developing novel assays and devices for diabetes diagnosis, treatment, and management. Currently, blood glucose detection is the standard method for diabetes diagnosis and management. However, other body fluids like saliva, urine, and sweat also contain glucose, which can be used for monitoring. Continuous glucose monitoring (CGM) devices linked with automated insulin delivery have become increasingly important, and their accuracy is crucial for delivering the right amount of insulin. Wearable sensing devices, including non-invasive glucose meters, have gained attention for real-time health monitoring. Although several commercial CGM products are available, their high cost limits their accessibility to the wider diabetes community. Advancements in nanotechnology, materials science, and biomedical engineering are expected to improve the development of affordable and accurate CGM devices, making them more accessible to those in need. The introduction of Continuous Glucose Monitoring (CGM) sensors has transformed glucose monitoring for Type 1 Diabetes Mellitus (T1DM) patients. Recent approvals and reimbursement policies have increased CGM adoption, with expectations of further growth as more affordable and less intrusive sensors become available. Future advancements are anticipated in CGM interoperability with devices like insulin pumps, activity trackers, and wearable sensors. Integrating CGM data with these devices will enhance glucose prediction algorithms and automated insulin modulation. Studies have shown promise in using CGM data to suspend basal insulin and develop artificial pancreas systems, particularly during exercise. This integration is expected to improve diabetes management and patient outcomes [21].

Conclusion

Wearable sensors hold significant potential for continuous, non-invasive monitoring of biomarkers for diabetes and other diseases. While many sensors require further clinical evaluation, existing devices like fitness bands and smartwatches provide a foundation for expansion into disease monitoring and diagnosis. Wearable continuous glucose monitoring (CGM) sensors are expected to revolutionize diabetes treatment. Decision support systems, implemented in software applications, can enhance their impact on patients' daily lives. Future developments may focus on low-cost devices, expanding the market to new populations, such as those with obesity and pre-diabetes. This could lead to new opportunities for industry and research. The acquisition of large amounts of CGM data and integration with other data sources, such as electronic health records and physical activity sensors, may enable the development of personalized, preventive, and proactive diabetes management strategies.

Author Contributions

All authors are contributed equally

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Declaration of Competing Interest

The Authors have no Conflicts of Interest to Declare.

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References

1. Clarke SF, Foster JR. A history of blood glucose meters and their role in self-monitoring of diabetes mellitus. British journal of biomedical science. 2012 Jan 1;69(2):83-93. **https://doi.org/10.1080/09674845.2012.12002443**
2. Ajjan RA, Cummings MH, Jennings P, Leelarathna L, Rayman G, Wilmot EG. Accuracy of flash glucose monitoring and continuous glucose monitoring technologies: implications for clinical practice. Diabetes and Vascular Disease Research. 2018 May;15(3):175-84. **https://doi.org/10.1177/1479164118756240**
3. Baumstark A, Schmid C, Pleus S, Rittmeyer D, Haug C, Freckmann G. Accuracy assessment of an advanced blood glucose monitoring system for self-testing with three reagent system lots following ISO 15197: 2013. Journal of Diabetes Science and Technology. 2014 Nov;8(6):1241-2. **https://doi.org/10.1177/1932296814546529**
4. Zisser HC, Bailey TS, Schwartz S, Ratner RE, Wise J. Accuracy of the SEVEN® continuous glucose monitoring system: comparison with frequently sampled venous glucose measurements. Journal of Diabetes Science and Technology. 2009 Sep;3(5):1146-54. **https://doi.org/10.1177/193229680900300519**
5. Shukla, S. K., Govender, P. P., & Tiwari, A. (2016). Polymeric micellar structures for biosensor technology. In Advances in biomembranes and lipid self-assembly (Vol. 24, pp. 143-161). Academic Press. **https://doi.org/10.1016/bs.abl.2016.04.005**
6. Benjamin EM. Self-monitoring of blood glucose: the basics. Clinical diabetes. 2002 Jan 1;20(1):45-7. **https://doi.org/10.2337/diaclin.20.1.45**
7. Gifford R. Continuous glucose monitoring: 40 Years, what we' ve learned and what's next. ChemPhysChem. 2013 Jul 22;14(10):2032-44. **https://doi.org/10.1002/cphc.201300172**
8. Bailey TS, Ahmann A, Brazg R, Christiansen M, Garg S, Watkins E, Welsh JB, Lee SW. Accuracy and acceptability of the 6-day Enlite continuous subcutaneous glucose sensor. Diabetes technology & therapeutics. 2014 May 1;16(5):277-83. **https://doi.org/10.1089/dia.2013.0222**
9. McGarraugh G, Brazg R, Weinstein R. FreeStyle Navigator Continuous Glucose Monitoring System with TRUstart algorithm, a 1-hour warm-up time. Journal of Diabetes Science and Technology. 2011 Jan;5(1):99-106. **https://doi.org/10.1177/193229681100500114**
10. Wong JC, Foster NC, Maahs DM, Raghinaru D, Bergenstal RM, Ahmann AJ, Peters AL, Bode BW, Aleppo G, Hirsch IB, Kleis L. Real-time continuous glucose monitoring among participants in the T1D Exchange clinic registry. Diabetes Care. 2014 Oct 1;37(10):2702-9. **https://doi.org/10.2337/dc14-0303**
11. Bequette BW. Continuous glucose monitoring: real-time algorithms for calibration, filtering, and alarms. Journal of diabetes science and technology. 2010 Mar;4(2):404-18. **https://doi.org/10.1177/193229681000400222**
12. Klonoff AN, Lee WA, Xu NY, Nguyen KT, DuBord A, Kerr D. Six digital health technologies that will transform diabetes. Journal of diabetes science and technology. 2023 Jan;17(1):23949. **https://doi.org/10.1177/19322968211043498**

13. Davidson PC, Hebblewhite HR, Steed RD, Bode BW. Analysis of guidelines for basal-bolus insulin dosing: basal insulin, correction factor, and carbohydrate-to-insulin ratio. Endocrine Practice. 2008 Dec 1;14(9):1095-101. **https://doi.org/10.4158/EP.14.9.1095**
14. Smart CE, King BR, McElduff P, Collins CE. In children using intensive insulin therapy, a 20-g variation in carbohydrate amount significantly impacts on postprandial glycaemia. Diabetic Medicine. 2012 Jul;29(7):e21-4. **https://doi.org/10.1111/j.1464-5491.2012.03595.x**
15. Pańkowska E, Ładyżyński P, Foltyński P, Mazurczak K. A randomized controlled study of an insulin dosing application that uses recognition and meal bolus estimations. Journal of diabetes science and technology. 2017 Jan;11(1):43-9. **https://doi.org/10.1177/1932296816683409**
16. Kovatchev BP, Breton M, Dalla Man C, Cobelli C. In silico preclinical trials: a proof of concept in closed-loop control of type 1 diabetes. **https://doi.org/10.1177/193229680900300106**
17. Diabetes Research in Children Network (DirecNet) Study Group. Use of the DirecNet Applied Treatment Algorithm (DATA) for diabetes management with a real-time continuous glucose monitor (the FreeStyle Navigator). Pediatric diabetes. 2008 Apr;9(2):142-7. **https://doi.org/10.1111/j.1399-5448.2007.00301.x**
18. O'Connor PJ, Sperl-Hillen JM, Fazio CJ, Averbeck BM, Rank BH, Margolis KL. Outpatient diabetes clinical decision support: current status and future directions. Diabetic Medicine. 2016 Jun;33(6):734-41. **https://doi.org/10.1111/dme.13090**
19. Jia P, Zhao P, Chen J, Zhang M. Evaluation of clinical decision support systems for diabetes care: an overview of current evidence. Journal of evaluation in clinical practice. 2019 Feb;25(1):66-77. **https://doi.org/10.1111/jep.12968**
20. Zhong A, Choudhary P, McMahon C, Agrawal P, Welsh JB, Cordero TL, Kaufman FR. Effectiveness of automated insulin management features of the MiniMed® 640G sensor-augmented insulin pump. Diabetes technology & therapeutics. 2016 Oct 1;18(10):657-63. **https://doi.org/10.1089/dia.2016.0216**
21. DeBoer MD, Cherñavvsky DR, Topchyan K, Kovatchev BP, Francis GL, Breton MD. Heart rate informed artificial pancreas system enhances glycemic control during exercise in adolescents with T1D. Pediatric diabetes. 2017 Nov;18(7):540-6. **https://doi.org/10.1111/pedi.12454s**
22. Avinash M, Suryaprabha M, Sreekanth N, Dineshreddy B, Baburao CH. Advanced and Recent Emerging Trends in Insulin Drug Delivery Systems. International Journal of Bio-Pharma Research. 2012;1.