J Young Pharm, 2021; 13(1) : 19-24.
A multifaceted peer reviewed journal in the field of Pharmacy
www.jyoungpharm.org | www.phcog.net

Review Article

The Effect of Glucosamine With or Without Chondroitin Sulphate on Glucose Monitoring Parameters in Humans – A Systematic Review

Bama VV Menon[1,2,*], Rosnani Hashim[2], Zainol Akbar Zainal[2], Anandarajagopal Kalusalingam[1], Abdullah Khan[1], Tan Ching Siang[1]
[1]Centre of Excellence in Pharmaceutical Sciences, School of Pharmacy, KPJ Healthcare University College, Nilai, MALAYSIA.
[2]Faculty of Pharmacy, University of Cyber Jaya, Cyber Jaya, Selangor, MALAYSIA.

ABSTRACT

Musculoskeletal diseases that included OA was the second greatest contributor to disability as measured by years lived with disability. The goals of OA treatment are to reduce pain, improve function and quality of life and decrease disability. The objective of this systematic review is to summarise the findings of the effect of glucosamine with or without chondroitin sulphate on glucose monitoring parameters in humans. An English language literature search of electronic bibliographic databases such as Medline, Web of Science, Science Direct, Scopus and Cochrane since inception to June 2020 was conducted. Two reviewers independently analysed the studies for quality and content using the Downs and Black Checklist. The thirteen studies that were included in the review consists of randomised control trials (*n*=7), non-randomised control trials (*n*=3), prospective cohort studies (*n*=2) and pre-post studies (*n*=1). Five studies detected the effect of glucosamine on glucose parameters. Studies that recruited patients with baseline impaired glucose tolerance or insulin resistance were more likely to detect an effect on glucose metabolism. Patients taking glucosamine have a higher risk of diabetes especially those who have high baseline glucose levels or have diabetes or have impaired glucose tolerance. Only two studies investigated the effect of glucosamine on glucose parameters in patients having osteoarthritis.

Key words: Diabetes, Glucosamine, Glucose metabolism, Osteoarthritis, Systematic review.

Correspondence

Mrs. Bama VV Menon

Centre of Excellence in Pharmaceutical Sciences, School of Pharmacy, KPJ Healthcare University College, Nilai, MALAYSIA.

Phone: +60123864980

Email: bamamenon@kpjuc.edu.my

DOI: 10.5530/jyp.2021.13.4

INTRODUCTION

The estimate by the Global Burden of Disease 2010 was that 251 million people suffered from knee osteoarthritis (OA) worldwide. OA, a musculoskeletal related disease was the second greatest contributor of disability as measured by years lived with disability.[1] Data from the National Health Interview Survey estimated that 14 million people in the US have symptomatic knee OA (KOA), that included more than 3 million racial or ethnic minorities.[2] OA is usually considered a physiological part of aging and rarely associated with mortality in the elderly.[3]

Glucosamine is a dietary supplement widely used for OA especially of the knees. It is described as not only efficacious but also safe for many patients.[4] It is available over the counter as a nutraceutical in several countries and it is also available as a prescription pharmaceutical in Europe.[5,6] In the United States alone, glucosamine was the fourth most commonly used herbal/ dietary supplement by over five million people annually.[7]

Previous short-term research studies have shown that glucosamine sulphate is safer than standard therapy such as Non-steroidal Anti-inflammatory Drugs (NSAIDs), especially concerning the gastrointestinal tract.[8] However, there are concerns regarding the effect of glucosamine on glucose metabolism causing insulin resistance. This has been proven in several animal based studies.[9] More recent studies suggest that it may also affect the glucose transport and insulin resistance in humans, especially when impaired glucose tolerance is present.[10–12] However, these studies differed in terms of the route of administration, duration as well as dosage of glucosamine. This review was aimed to summarise the findings of the use of glucosamine with or without chondroitin at pharmacological doses and its effect on glucose monitoring parameters in humans.

MATERIALS AND METHODS

This review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). Studies were located through a comprehensive literature search of electronic bibliographic databases such as Medline, Web of Science, Science Direct, Scopus and Cochrane since inception to June 2020. These databases were searched for intervention trials investigating the effects of glucosamine alone or in combination with chondroitin on glucose monitoring parameters such as HbA_{1c}, fasting plasma glucose, fasting insulin levels, fructosamine and other relevant parameters. Studies were selected for review as per Diagram 1.

Search Strategy

The subject headings (SH) and keywords used are based on the aspects of the PICO framework such as osteoarthritis, temporomandibular Joint and arthritis for the population; glucosamine and chondroitin as the intervention and hyperglycaemia, fructosamine, insulin resistance, glucose tolerance test and glucose toxicity as part of the outcomes.

The search was conducted by a combination (using Boolean operators) of the search terms. Search limiters were English language, human

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

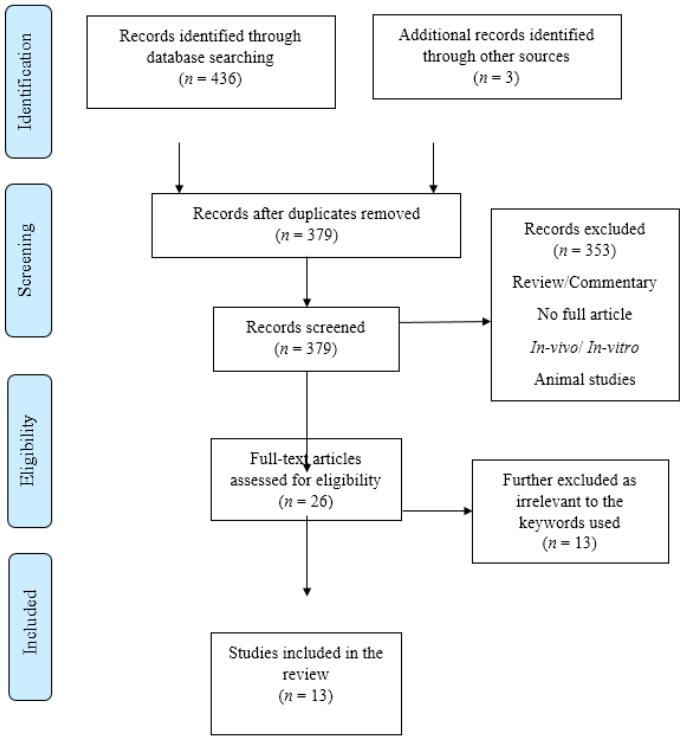

Diagram 1: PRISMA 2009 Flow Diagram.

subjects and journal articles. Reference lists of selected articles were also sourced manually to gain more insight. Chosen articles were exported into Mendeley and checked for duplicates.

Inclusion Criteria

- All published types of studies and trials
- Only English language articles
- On treatment with glucosamine and chondroitin or glucosamine alone.
- There were no restrictions in age, health, gender, body mass index (BMI) or disease comorbidities.
- All types of glucosamine and administration by any route.
- All possible methods of glucose monitoring parameters

Exclusion Criteria

- All *in-vitro* and *in-silico* studies
- Animal studies
- Single measurements of random or fasting glucose

Quality Assessment

Each selected study was assessed for quality using the Downs and Black Checklist.[13] This checklist includes 27 criteria, widely covering areas reporting quality, external and internal validity and power. The quality of each study was independently assessed by two reviewers, with discrepancies resolved through discussion and consensus.

RESULTS

Study Selection

A total of 426 articles were traced from the databases and 3 articles were obtained manually. After de-duplication, 379 articles proceeded for screening and 353 articles were excluded as per exclusion criteria. Of 26 articles that were checked for eligibility, 14 articles were appraised and finally, 13 were included in the review. The summary of the 13 studies are shown (Table 1). The studies that were included in the review consisted of randomised control trials (*n*=7), non-randomised control trials (*n*=3), prospective cohort studies (*n*=2) and pre-post studies (*n*=1). Nine of the studies used multiple glucosamine dosing while four studies used single glucosamine dosing.

Appraisal of Studies

The research articles selected were scrutinised and assessed using the Downs and Black checklist[13] and compiled (Table 2). Out of the 14 papers, one was assessed to be poor due to the fulfilment of only 4 out of 27 criteria.[14] This paper was later removed from the review group of studies. Five studies were assessed as Fair[15-19] while 6 articles scored as Good.[11,17–21] Two of the studies fulfilled 26 and 27 criteria and scored excellent.[22,23]

Sample Size and Characteristics

Patients or respondents were from the US, Canada, Netherlands, UK, Iran and Iraq. Only one of the studies which was a cohort study involved the biggest sample size, which was 404,508 participants.[21] Two studies recruited diabetic subjects[20,23] while two studies included subjects who had impaired glucose tolerance.[20,24] Seven studies recruited only healthy subjects.[11,15-17,21,22,25] Only two studies recruited osteoarthritic patients.[19,26]

One study randomised the subjects according to obesity status i.e. lean and obese categories.[17] Five of the studies merely reported the mean BMI[10,15,17,18,21] from which three of the studies reflected that the subjects were mostly obese as the mean BMI was more than 30.[18,22,23]

Glucosamine Dosing

Six of the studies followed the recommendation of dosing in the CPG Management of Osteoarthritis 2nd Ed 2013[11,18-20,22,26] while one prospective study reported affirmative use of glucosamine but no specific information provided on the dosing.[21] Three of the studies used the recommended dose but at a shorter duration of between 14 to 42 days.[17,23,24] Nine studies used multiple dosing of glucosamine[11,17,19-24,26] while four studies tested single doses of glucosamine.[15-16,18,25]

Measured Outcome

As shown in Table 3, out of the thirteen studies, only six used HbA_{1c} as an outcome,[11,17,20,22,24,26] four of which were RCTs.[11,17,20,22] Fasting glucose was used as a measuring parameter in most studies.[11,15-19,23-36] Three out of the thirteen studies measured OGTT as a parameter.[11,18,19] In order to determine insulin resistance, eight studies performed fasting insulin test as a secondary outcome.[11,15-19,24,25]

Another similar study included a euglycemic insulin clamp and found no effects on glucose metabolism. In fact, the total body insulin sensitivity and whole body glucose uptake following glucosamine were similar to those of placebo. In addition, glucosamine did not affect the arteriovenous blood glucose difference or forearm glucose uptake.[16]

One of the studies showed a significant effect on glucose monitoring parameters whereby the HOMA value rose after 6 weeks of daily glucosamine and the QUICKI index plunged in the same duration. Therefore, the effect of glucosamine on glucose or insulin was significant in the patients with higher baseline insulin resistance.[24]

Despite no significant effect of oral glucosamine on glucose metabolism in normoglycemic people, three of the patients with abnormal glucose tolerance tests showed a higher glucose AUC increment.[18] This is the first study to report glucose and insulin levels when glucosamine is ingested together with an oral glucose load.

Table 1: Summary of Studies Done on the Effect of Glucosamine on Glucose Monitoring Parameters in Humans.

Study	Design (Placebo)	Study Subject					BMI (kg/m^2)	Glucosamine/ Chondroitin	Measured Outcomes	Findings	Consideration Points	Respondent Origin
		N	H	IGT	DM	OA						
Scroggie (2003)	RCT/DB (Placebo)	34	0	0	34		N/A	1500 mg OD X 90 days (hydrochloride)	HbA_{1c}	Not significant.	Not OA subjects	US
Tannis (2004)	RCT/DB (placebo)	19	19	0	0		: 25.5	1500 mg OD X 84 days (sulphate)	Fasting glucose Fasting insulin OGTT (3h) HbA_{1c}	Not significant	Not OA subjects	Canada
Muniyappa (2006)	RCT/DB/ Cross over (placebo)	40	40				Obese (20) : 34.2 Lean (20) : 24.3	1500 mg OD X 42 days (hydrochloride)	Fasting glucose Fasting insulin HbA_{1c} QUICKI Clamp	Not significant	Not OA subjects	US
Albert (2007)	RCT/DB/ Cross over (placebo)	12	0	0	12		: 36.7	1500 mg OD X 14 days	Fasting glucose Fructosamine	Not significant	Not OA subjects	US
Pham (2007)	Pre-Post study (No Placebo)	38	31	7	0		: 29.1	1500 mg OD X 42 days	Fasting glucose Fasting insulin HbA_{1c} HOMA/QUICKI	Significant	Not OA subjects	US
Al Razuqqi (2011)	Prospective Open study	93		0	0	93	N/A	1500 mg OD X 91 days/ 1200 mg /day X91 days	Fasting glucose HbA_{1c}	Significant (normoglycemic with female familial history of diabetes)	BMI not done	Iraq
Saghafi (2016)	RCT/ DB(Placebo)	40				40	N/A	1500 mg OD X 90 days (sulphate)	Fasting glucose Fasting Insulin OGTT HOMA-IR	Not significant	BMI not done	Iran
Gommans (2016)	RCT/DB (Placebo)	407	407	0	0		: 32	1500 mg OD X 2.5 years (912.5 days)	HbA_{1c}	Not significant	Not OA subjects	Netherlands
Ma (2020)	Prospective Cohort Study	404 508	404 508				< 18.5: 2157 18.5-24.9: 138295 25-29.9: 174763 ≥30: 89293	N/A	Blood glucose CRP	Habitual glucosamine use is associated with a lower risk of T2D.	Not OA patients	UK
Monauni (2000)	RCT/ Cross over (placebo)	10	10				: 23.5	IV 1.6 µmol/min/kg X 300 min (all) 5 Umol/min/kg X 300 min (n=5)	Fasting glucose IVGTT Clamp Fasting insulin	Increased fasting glucose; Decreased insulin sensitivity (IVGTT)	Not OA patients	Italy

Pouwels (2001)	Control (placebo)	20	20		: 22.3	IV 4 mmol/dL X 150 min (n=6) or 300 min (n= 6) Placebo : 8 (sulphate)	Fasting glucose Fasting insulin Clamp	Not significant	Not OA patients	Netherlands
Laferrere (2004)	Control (placebo)	20	20		N/A (20.8-29.5)	Oral GS 3000 mg X 1 dose (n=6) Oral GS 6000 mg X 1 dose (n=5) Placebo: 9 (sulphate)	Fasting glucose Fasting insulin Leptin	Not significant	Not OA patients	US
Biggee (2007)	Control, cross over (placebo)	16	13	3	: 31	Oral 1500 mg X 1 dose (sulphate)	Fasting glucose Fasting insulin Random insulin OGTT (2 and 3 h)	Decreased insulin sensitivity in subjects with IGT/ DM (OGTT)	Not OA patients	US

RCT-Randomised Controlled Trial, DB-Double blinded, N-number of subjects, H-healthy, IGT-Impaired Glucose Tolerance, DM-diabetes mellitus, OA-osteoarthritis, OD-once daily, HbA_{1c}-glycosylated Hemoglobin, OGTT-oral glucose tolerance test, CRP-C-reactive protein, IVGTT-intravenous glucose tolerance test, GS-glucosamine sulphate, QUICKI-Quantitative Insulin Sensitivity Check Index, T2D- Type 2 diabetes, HOMA-Homeostatic Model Assessment, HOMA-IR-Homeostatic Model Assessment for Insulin Resistance.

Effect on Glucose Metabolism

Of the thirteen studies, only four studies detected an effect on glucose parameters. Two studies concluded that the use of glucosamine significantly impaired the glucose parameters.[24,26] The use of glucosamine at therapeutic doses may worsen insulin resistance and vascular function in subjects with underlying poorer insulin sensitivity.[24] Normoglycemic patients with a family history of diabetes (especially female relatives) should use glucosamine-chondroitin supplements with caution.[26] One study detected increased fasting glucose and decreased insulin sensitivity tested using IVGTT[15] while another study detected decrease insulin sensitivity in patients with IGT using OGTT[24] Conversely, habitual use of glucosamine was associated with a 17% lower risk of T2DM, independent of the traditional risk factors for T2DM, socio-economic factors and use of supplements other than glucosamine.[21]

DISCUSSION

The sample sizes of subjects were small[10,13–23] except for a prospective cohort study which involved 404,508 subjects.[21] Duration of study ranged between 14 and 90 days. The prospective study focussed on long term effects of glucosamine and its association with T2DM, hence the follow- up period of 8.1 years.[21] The shortest duration of the trial was only 14 days.[23] Two of the studies were for a duration of 90 days[19,20] while two more were for 42 days.[17,24] The longest duration was 8.1 years.[21] The study design was also different as it was a prospective cohort study. The usual therapeutic dose of glucosamine as per recommendation in the CPG Management of Osteoarthritis 2nd Ed 2013 is 1500 mg daily for 3 months or more.[27] Efficacy with relation to symptoms improvement is usually observed after 12 weeks.[27] Therapeutic effects are obtained with doses ranging between 1,250–1,500mg daily.[28] Symptomatic slow-acting drugs for OA (SYSADOA) such as glucosamine offer a slow onset of relief-approximately 2 weeks-but their effects may remain active for as long as 2 months after their omission.[28]

In terms of quality, all the 13 studies scored between 8 – 10 points in the reporting section of the Downs and Black Checklist. Eight of the studies scored a full score for external validity.[17-23,25] Five studies scored full for internal validity[17,19,20,22,23] while one study scored the lowest.[25] One study scored the highest for internal validity (selection bias)[22] which reflects the least biasness. Despite having small sample sizes, three of the studies had sufficient power to detect a clinically important effect with the probability being less than 5%.[15,20,23] Of the three, only one detected significant effect on fasting glucose,[15] but glucosamine administration was by injection, which is not a normal route of administration.

A study focusing on the effect of glucosamine on insulin secretion found that plasma glucose concentrations increased after 40–60 min infusions of glucosamine, regardless of dose; however, high dose infusions worsened intravenous glucose tolerance.[29] Further, only high-dose glucosamine reduced glucose clearance and blunted insulin sensitivity and glucose effectiveness.[12]

Seven out of twelve studies done have shown a significant association between diabetes and osteoarthritis.[30] Different studies had demonstrated the relationship between chronic DM and rapid progression of OA with higher rates of synovial inflammation and joint pain. Conversely, the relationship between OA and DM appears to be bidirectional.[31] In a cohort study, joint pain and reduced mobility in the knee and hip, leading to a sedentary lifestyle have demonstrated to significantly promote the development of T2DM in patients older than 55 years of age.[32] Apart from that, the possibility of glucosamine inducing diabetes is widely seen in OA patients as they use glucosamine as a symptom and structure modifying agent.[8] More studies should be conducted on

Table 2: Downs and Black Checklist Summary.

Study	Reporting (11)	External Validity (3)	Internal Validity (7)	Selection Bias (6)	Power of Study (1)	Total (28)	Outcome
Gommans, 2016	10	3	7	6	1	27	Excellent
Albert, 2007	10	3	7	5	1	26	Excellent
Saghafi, 2016	10	3	7	5	0	25	Good
Muniyappa, 2006	10	3	7	5	0	25	Good
Scroggie, 2003	8	3	7	5	1	24	Good
Tannis, 2004	10	1	6	4	0	21	Good
Ma, 2020	10	3	4	3	0	20	Good
Biggee, 2007	9	3	5	3	0	20	Good
Pham, 2007	10	1	5	3	0	19	Fair
Al-Razuqqi, 2011	9	2	5	2	0	18	Fair
Monauni, 2000	8	1	5	2	1	17	Fair
Pouwels, 2001	9	0	5	2	0	16	Fair
Laferrere, 2004	8	3	3	2	0	16	Fair

Table 3: Summary of Measured Outcome.

Glucose Related Parameters	Multiple dosing (9)	Single dosing (4)	N
HbA_{1c}	6	0	6
Fasting glucose	7	4	11
Fasting Insulin	5	4	9
Random glucose	1	0	1
Random Insulin	0	1	1
Glucose Tolerance Test	3	2	5
HOMA-IR	2	0	2
Meal Tolerance Test	1	0	1
Clamp	1	2	3
QUICKI	2	0	2

osteoarthritic patients taking glucosamine in order to determine an accurate relationship between glucosamine and diabetes.

In terms of efficacy of oral glucosamine in the management of OA, four large scale RCTs have been carried out.[33-37] These studies were conducted for a duration period of between 6 months and 3 years and included about over 2000 subjects. However, these studies measured only random blood glucose and did not specifically address the glucose metabolism problem. None of these studies reported an adverse effect on glucose metabolism among subjects taking glucosamine. However, it is inconclusive to say that glucosamine does not affect glucose metabolism as these studies were not designed to appropriately assess glucose metabolism.

Another interesting finding is that insulin resistance is often observed in obese people. Obesity is a risk factor for both OA and DM. For instance, the association of obesity with OA is well documented,[29] and obesity occurs in the majority of people with T2DM.[38] Therefore, in obese patients taking glucosamine, there is always a risk of developing DM.

There was no clear association between the use of glucosamine and the occurrence of diabetes or glucose related toxicities. In addition, the type of glucosamine (sulfate or hydrochloride), the brand may contribute to the effect on glucose parameters. One review revealed that only Rottapharm glucosamine significantly improved pain and functional limitations in OA patients.[5] This implied that the brand could cause a different effect on glucose metabolism. Nevertheless, none of the studies revealed the brand of glucosamine. Besides the brand, the standard regiment and the subjects recruited also play a role in the determination of effect on glucose metabolism. For instance, the effect of glucosamine on OA patients, who are more likely to be on glucosamine and share similar risk factors for diabetes would be different than healthy subjects.

The limitations of the studies chosen were the underestimation of the effect of glucosamine on diabetic patients with normal HbA_{1c},[22] the use of glucosamine being a marker for healthy lifestyle,[21] the absence of measurement of glucosamine levels and its metabolites,[25] the use of the HOMA-IR model for assessment of insulin resistance when the glucose clamping technique is considered the gold standard for assessing insulin resistance and also small sample size which limited the statistical results of the study.[19]

CONCLUSION

From the review, it can be concluded that there were inadequate studies to establish a link between glucosamine and glucose metabolism. Studies done varied in terms of the type of subjects, dose and duration. There is a need for studies to mimic the actual use of glucosamine amongst OA patients for a minimum of at least 3 months at the dose recommended by the guidelines and capture the exact effect on glucose parameters such as fasting glucose or HbA_{1c}. So far, some evidences point to the increased risk of DM in patients who have high baseline glucose levels, or have diabetes or have impaired glucose tolerance. Ideally, the effect of glucosamine should be investigated on OA patients with baseline IGT or with family history of DM for better risk management.

ACKNOWLEDGEMENT

We acknowledge the Centre of Excellence, School of Pharmacy, KPJ Healthcare University College, MALAYSIA.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

AUC: Area under curve; **OA:** Osteoarthritis; **HbA_{1c}:** Glycosylated hemoglobin; **OGTT:** Oral glucose tolerance test; **IVGTT:** Intravenous glucose tolerance test.

REFERENCES

1. Vos T, Flaxman AD, Naghavi M, *et al*. Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990-2010: A systematic analysis for the Global Burden of Disease Study 2010. Lancet. 2012;380(9859):2163-96. doi:10.1016/S0140-6736(12)61729-2
2. Vina ER, Kent KC. Epidemiology of Osteoarthritis: Literature Update Ernest. Physiol Behav. 2018;30(2):160-7. doi:10.1016/j.gde.2016.03.011
3. Hootman JM, Helmick CG, Brady TJ. A public health approach to addressing arthritis in older adults: The most common cause of disability. Am J Public Health. 2012;102(3):426-33. doi:10.2105/AJPH.2011.300423
4. Lee YH, Woo JH, Choi SJ, Ji JD, Song GG. Effect of glucosamine or chondroitin sulfate on the osteoarthritis progression: A meta-analysis. Rheumatol Int. 2010;30(3):357-63. doi:10.1007/s00296-009-0969-5
5. Towheed T, Maxwell L, Tp A, *et al*. Glucosamine therapy for treating osteoarthritis. Cochrane Database of Systematic Reviews. 2009;(4).
6. Hochberg MC, Altman RD, April KT, *et al*. American College of Rheumatology 2012 recommendations for the use of nonpharmacologic and pharmacologic therapies in osteoarthritis of the hand, hip and knee. Arthritis Care Res. 2012;64(4):465-74. doi:10.1002/acr.21596
7. Stumpf JL, Lin SW. Effect of glucosamine on glucose control. Ann Pharmacother. 2006;40(4):694-8. doi:10.1345/aph.1E658
8. Bruyère O, Altman RD, Reginster JY. Efficacy and safety of glucosamine sulfate in the management of osteoarthritis: Evidence from real-life setting trials and surveys. Semin Arthritis Rheum. 2016;45(4):S12-7. doi:10.1016/j.semarthrit.2015.11.011
9. Hussain MA. A case for glucosamine. Eur J Endocrinol. 1998;139(5):472-5. doi:10.1530/eje.0.1390472
10. Simon RR, Marks V, Leeds AR, Anderson JW. A comprehensive review of oral glucosamine use and effects on glucose metabolism in normal and diabetic individuals. Diabetes Metab Res Rev. 2011;27(1):14-27. doi:10.1002/dmrr.1150
11. Tannis AJ, Barban J, Conquer JA. Effect of glucosamine supplementation on fasting and non-fasting plasma glucose and serum insulin concentrations in healthy individuals. 2004;12(6):506-11. doi:10.1016/j.joca.2004.03.001
12. Dostrovsky NR, Towheed TE, Hudson RW, Anastassiades TP. The effect of glucosamine on glucose metabolism in humans: A systematic review of the literature. Osteoarthr Cartil. 2011;19(4):375-80. doi:10.1016/j.joca.2011.01.007
13. Validity E. Downs and Black 1998 The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health. 1998;52(6)377-84.
14. Yu JG, Boies SMOJ. The Effect of Oral Glucosamine Sulfate on Insulin Sensitivity in Human Subjects. Diabetes Care. 2003;26(6):1941-2.
15. Monauni T, Zenti MG, Cretti A, et al. Effects of glucosamine infusion on insulin secretion and insulin action in humans. Diabetes. 2000;49(6):926-35. doi:10.2337/diabetes.49.6.926
16. Pouwels MJ, Jacobs JR, Span PN, et al. Short-Term Glucosamine Infusion Does Not Affect Insulin Sensitivity in Humans *. Journa Clin Endrocrinology Metab. 2001;86(5):2099-103.
17. Muniyappa R, Karne RJ, Hall G, *et al*. Oral glucosamine for 6 weeks at standard doses does not cause or worsen insulin resistance or endothelial dysfunction in lean or obese subjects. Diabetes. 2006;55(11):3142-50. doi:10.2337/db06-0714
18. Biggee BA, Blinn CM, Nuite M, Silbert JE, McAlindon TE. Effects of oral glucosamine sulphate on serum glucose and insulin during an oral glucose tolerance test of subjects with osteoarthritis. Ann Rheum Dis. 2007;66(2):260-2. doi:10.1136/ard.2006.058222
19. Saghafi M, Karimi M, Bonakdaran S, Massoudnia N. Oral glucosamine effect on blood glucose and insulin levels in patients with non-diabetic osteoarthritis: A double-blind, placebo-controlled clinical trial. Arch Rheumatol. 2016;31(4):340-5. doi:10.5606/ArchRheumatol.2016.5632
20. Scroggie DA, Albright A, Harris MD. The effect of glucosamine-chondroitin supplementation on glycosylated hemoglobin levels in patients with type 2 diabetes mellitus: A placebo-controlled, double-blinded, randomized clinical trial. Arch Intern Med. 2003;163(13):1587-90. doi:10.1001/archinte.163.13.1587
21. Ma H, Li X, Zhou T, et al. Glucosamine use, inflammation and genetic susceptibility and incidence of type 2 diabetes: A prospective study in UK Biobank. Diabetes Care. 2020;43(4):719-25. doi:10.2337/dc19-1836
22. Gommans YMM, Runhaar J, Jacobs ML. The effect of prolonged glucosamine usage on HbA1c levels and new-onset diabetes mellitus in overweight and obese middle-aged women. Am J Med. 2017. doi:10.1016/j.amjmed.2016.11.038
23. Albert GS, Oiknine RFPS, et al. The Effect of Glucosamine on Serum HDL Cholesterol and Apolipoprotein AI Levels. Diabetes Care. 2007;30(11):2800-3. doi:10.2337/dc07-0545.Abbreviations
24. Pham T, Cornea A, Blick KE, Jenkins A, Scofield RH. Oral glucosamine in doses used to treat osteoarthritis worsens insulin resistance. Am J Med Sci. 2007;333(6):333-9. doi:10.1097/MAJ.0b013e318065bdbe
25. Laferrere B, Garcia-Lorda P, Russel CD P-SFX. Effect of Oral Glucosamine Sulfate on Serum Leptin Levels in Human Subjects. Nutrition. 2004;20(3):321-2. doi:10.1016/j.nut.2003.11.010
26. Al-Razzuqi RAM, Al-Jeboori AA. Is glucosamine-chondroitin risky to normoglycemic individuals with family history of diabetes mellitus. Int J Diabetes Dev Ctries. 2011;31(1):37-40. doi:10.1007/s13410-010-0012-0
27. Melorose J, Perroy R, Careas S. CPG Management of Osteoarthritis (2nd Ed). Vol 2.; 2013. doi:10.1017/CBO9781107415324.004
28. Black C, Clar C, Henderson R, et al. The clinical effectiveness of glucosamine and chondroitin supplements in slowing or arresting progression of osteoarthritis of the knee: A systematic review and economic evaluation. Health Technol Assess. 2009;13(52):1-123. doi:10.3310/hta13520
29. Scott RA, Langenberg C, Sharp SJ, et al. The link between family history and risk of type 2 diabetes is not explained by anthropometric, lifestyle or genetic risk factors: The EPIC-InterAct study. Diabetologia. 2013;56(1):60-9. doi:10.1007/s00125-012-2715-x
30. Louati K, Vidal C, Berenbaum F, Sellam J. Association between diabetes mellitus and osteoarthritis: Systematic literature review and meta-analysis. RMD Open. 2015;1(1). doi:10.1136/rmdopen-2015-000077
31. Cannata F, Vadalà G, Ambrosio L, et al. Osteoarthritis and type 2 diabetes: From pathogenetic factors to therapeutic intervention. Diabetes Metab Res Rev. 2020;36(3):1-15. doi:10.1002/dmrr.3254
32. Kendzerska T, King LK, Lipscombe L, Croxford R, Stanaitis I, Hawker GA. The impact of hip and knee osteoarthritis on the subsequent risk of incident diabetes: A population-based cohort study. Diabetologia. 2018;61(11):2290-9. doi:10.1007/s00125-018-4703-2
33. Clegg DOOJR. Glucosamine, Chondroitin Sulfate and the Two in Combination for Painful Knee Osteoarthritis. N Engl J Med. 2006;354(8):795-808.
34. Herrero-Beaumont G, Román Ivorra JA, Trabado MDC, et al. Glucosamine sulfate in the treatment of knee osteoarthritis symptoms: A randomized, double-blind, placebo-controlled study using acetaminophen as a side comparator. Arthritis Rheum. 2007;56(2):555-67. doi:10.1002/art.22371
35. Reginster JY, Deroisy R, Rovati LC, et al. Long-term effects of glucosamine sulphate on osteoarthritis progression: A randomised, placebo-controlled clinical trial. Lancet. 2001;357(9252):251-6. doi:10.1016/S0140-6736(00)03610-2
36. Pavelká K, Gatterová J, Olejarová M, Machacek S, Giacovelli G, Rovati LC. Glucosamine Sulfate Use and Delay of Progression of Knee Osteoarthritis. Arch Intern Med. 2002;162(18):2113. doi:10.1001/archinte.162.18.2113
37. Veronese N, Cooper C, Reginster JY, et al. Type 2 diabetes mellitus and osteoarthritis. Semin Arthritis Rheum. 2019;49(1):9-19. doi:10.1016/j.semarthrit.2019.01.005
38. Teodoro JS, Varela AT, Rolo AP, Palmeira CM. High-fat and obesogenic diets: Current and future strategies to fight obesity and diabetes. Genes Nutr. 2014;9(4). doi:10.1007/s12263-014-0406-6.

Article History: Submission Date : 24-11-2020; Revised Date : 16-12-2020; Acceptance Date : 09-01-2021
Cite this article: Menon BVV, Hashim R, Zainal ZA, Kalusalingam A, Khan A, Siang TC. The Effect of Glucosamine with or Without Chondroitin Sulphate on Glucose Monitoring Parameters in Humans–A Systematic Review. J Young Pharm. 2021;13(1):19-24.