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Antidiabetic Activity of *Momordica charantia* Fruit Extract in Streptozotocin-Induced Diabetic Rats

Florian Moser¹●, Divya Srivastava²●, Wout Cuvelier³●

¹Scientist, Department of Pharmaceutics, Salzkammergut Institute of Immunology, Gmunden, Austria.

²Senior Research Fellow, Department of Pharmaceutics, Nallamala Institute of Life Sciences, Kurnool, India.

³Research Associate, Department of Pharmaceutics, Ardennes Centre for Genetics, Bastogne, Belgium.

Email: ¹f.moser@sii-g.at, ²d.srivastava@nils.ac.in, ³w.cuvelier@acg-b.be

ORCID: ¹0000-0001-3303-8070, ²0000-0001-1019-7546, ³0000-0001-0068-7621

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ABSTRACT

Bitter melon, the fruit of *Momordica charantia*, is among the most widely used traditional remedies for diabetes, and reports of its glucose-lowering effect in streptozotocin-induced diabetic rats are common. This narrative review asks what such reports can and cannot establish. It draws on published work on the chemistry and proposed mechanisms of the fruit, on how streptozotocin damages pancreatic beta cells, on the design and reporting of rodent studies, and on the small human literature, and it presents no new data and no local experiment. The fruit contains several groups of compounds, including cucurbitane triterpenoids and protein fractions, with plausible actions on glucose uptake, insulin release and hepatic glucose output, yet most proposed mechanisms rest on cell work or on single animal studies. Streptozotocin models are convenient, but the degree of beta-cell loss, the timing of confirmation, spontaneous recovery and the choice of extract all shape the outcome. Weak points of the reporting, notably small groups, unclear randomisation and blinding, undefined extracts and treating cages as independent units, limit how far a positive result can travel. A glucose-lowering effect in the rat is plausible and often reproduced in direction, but its size, its mechanism and its relevance to people remain unsettled. The review closes with the features a convincing study of a fruit extract in this model would contain.

Keywords: *Momordica charantia*; Bitter melon; Streptozotocin; Diabetic rat; Antidiabetic plants; Experimental design; Narrative review

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Article Class: Narrative Review

1. Introduction

Diabetes mellitus is now one of the commonest chronic diseases worldwide, and estimates made over the last decade point to a steady rise in the number of

affected adults, much of it in low- and middle-income countries (1, 2). Type 2 diabetes, the dominant form, reflects a failing partnership between insulin resistance in muscle, liver and fat and a



gradual decline in beta-cell function (3, 4). Where medicines are costly or hard to reach, many people turn to plants (5, 6).

Among these plants the fruit of *Momordica charantia*, known as bitter melon, bitter gourd or karela, holds a special place. Its use in Asia, Africa and South America is described in several reviews (7, 8, 9), and papers reporting that an extract of the fruit lowers blood glucose in streptozotocin-induced diabetic rats appear regularly. This article does not add another such experiment. It is a narrative review of the published literature on the topic named in its title, and no data from any local study, laboratory or animal facility are reported here. The question is how much a positive result in this particular model can be trusted, and for what. The aim is to separate what has been shown from what is merely repeated.

2. Literature Review

2.1 Bitter Melon and Its Constituents

The fruit is a rich and untidy chemical mixture. Reviews list cucurbitane-type triterpenoids, sterol glycosides often grouped as charantin, several protein fractions, saponins and flavonoids (7, 9). A polypeptide with insulin-like activity, usually called polypeptide-p, was described in the early 1980s from the fruit and seeds and reported to lower glucose in animals and in a small number of people (10). Later work on isolated triterpenoids showed activation of AMP-activated protein kinase in cells and in rodents, a pathway that fits the idea of greater glucose uptake in muscle and fat (11, 12). No single compound has been shown to account for the activity of the whole fruit, and it is not clear that any one of them works as well alone as in combination.

Seeds contain vicine, which has been linked to favism in susceptible people, and case reports describe low glucose in

children after bitter melon preparations (13). Variety, ripeness and the way the fruit is dried or extracted all change the balance of compounds, which is one reason chemical profiles in different papers do not line up. Table 1 summarises the main groups and how firmly each proposal stands. The level of support is uneven: much of it comes from cell work or from single animal reports.

Table 1. Compound groups reported from bitter melon and what has been proposed for them.

Compound group	Proposed action	Level of support
Cucurbitane triterpenoids	Activation of AMPK, more glucose uptake (11, 12)	Cell and animal work
Polypeptide-p and protein fractions	Insulin-like or secretagogue effect (10, 14)	Animal work, mixed
Sterol glycosides (charantin)	Glucose lowering after oral dosing (7, 8)	Old, weakly characterised
Crude fruit extracts	Lower glucose and lipids in rodents (15, 16)	Many reports, varied extracts
Seeds and vicine	Adverse effects in some people (13)	Case reports

Note: Qualitative summary of published proposals; content of each group varies with variety, ripeness and extraction.

2.2 Proposed Mechanisms of Glucose Lowering

Several routes have been put forward (Figure 1). A protein extract from the fruit pulp stimulated insulin release and behaved like insulin in some assays (14). Triterpenoid activation of AMPK would raise glucose uptake without needing much insulin (11). In animals fed a high-fat diet, bitter melon lowered adiposity and improved glucose tolerance, which suggests an action on insulin resistance and body fat as well as on glucose itself (17, 18). Reviews add hepatic glucose output, though this is less firmly



established (19, 20).

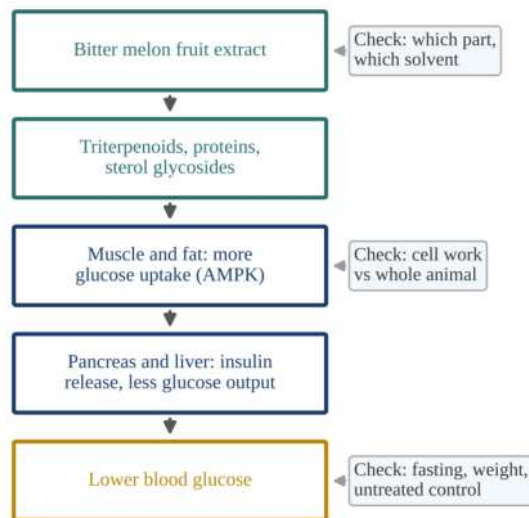


Figure 1. Proposed routes from bitter melon fruit to lower blood glucose, with the checks that apply to each (schematic, not data).

What is striking is how many mechanisms are claimed for one fruit. Either the plant is unusually versatile, or the mixture differs between preparations and each study has caught a different part of it. This is why the same plant can look excellent in one report and unremarkable in the next.

2.3 The Streptozotocin Model

Streptozotocin is a nitrosourea taken up by beta cells through the glucose transporter GLUT2. Inside the cell it alkylates DNA, sets off repair processes that exhaust cellular energy stores, and releases nitric oxide, so the cell dies (21). A single high dose destroys most beta cells and produces a state closer to type 1 diabetes, with little endogenous insulin left. Lower doses, sometimes combined with a high-fat diet or with nicotinamide given beforehand, leave part of the beta-cell mass intact and give a milder picture closer to type 2 (22, 23, 24).

This matters for plant extracts. An agent that works by stimulating insulin release will have little to act on in a rat whose beta cells are nearly gone, whereas an agent that

improves uptake in muscle could look effective in either version. Protocols also differ in strain, sex, fasting and the cut-off used to call an animal diabetic (25, 26). Reviews of diabetic animal models stress that none reproduces the human disease and that the choice should follow the question asked (27, 28). Such differences look small one at a time, but they add up across a literature.

2.4 Evidence in People

The human literature is small. A Cochrane review of bitter melon for type 2 diabetes found too little good evidence to recommend it, partly because the trials were few, short and variable in their preparations (29). A randomised comparison with metformin in people with newly diagnosed type 2 diabetes reported a glucose-lowering signal at the doses tested, but it did not settle the question of long-term benefit (30). A mini review reached a similar position: promising, uneven, and in need of larger and better-controlled trials (20, 31).

3. Materials and Methods

3.1 Scope

This is a narrative synthesis, not a systematic review. It covers the chemistry and proposed mechanisms of bitter melon, the streptozotocin rat model, the design and reporting of rodent studies of plant extracts, and the small human literature. It does not report any original experiment, and no animals were handled for it. It says nothing about any single institution or population.

3.2 Literature Assembly

Sources were gathered by reading widely rather than by a formal database search with fixed terms, and no protocol was registered. The starting points were the general reviews on bitter melon and on diabetic animal models, and the reference



lists of those papers were followed to the original studies and to the methodological literature. Relevant papers may therefore have been missed. None of these steps is difficult, but each one is easy to skip.

3.3 Appraisal Framework

Each body of work was read against a short set of questions listed in [Table 2](#). They draw on the ARRIVE reporting guideline, on a risk-of-bias tool built for animal studies, and on general advice about the design of animal experiments ([32](#), [33](#), [34](#)). No scores were calculated. The questions were used to decide how much weight a statement deserves and to separate what is observed from what is inferred. It is a habit worth keeping even when the answer seems obvious.

Table 2. Questions used to appraise a rodent study of a plant extract.

Question	What is looked for	Source
Was the model described?	Agent, route, timing, confirmation (25 , 26)	Model papers
Were animals allocated fairly?	Randomisation, concealment, blinding (33)	Risk-of-bias tool
Was the extract defined?	Part, solvent, yield, marker (32)	Reporting guideline
Was the unit right?	Cage or animal as unit (34 , 35)	Design papers
Were all results shown?	Attrition and null results (36)	Bias literature

Note: The questions follow the reporting and risk-of-bias guidance cited; they are used here as a reading aid, not as a scoring system.

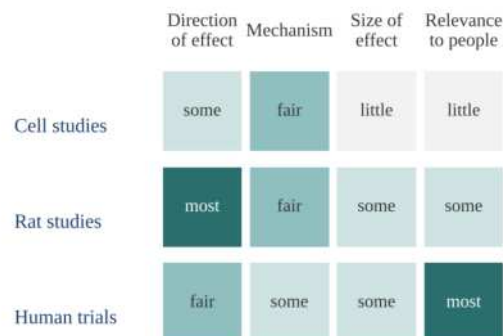
4. Results

4.1 What the Rat Studies Generally Report

Across the animal literature ([Figure 2](#)) the direction of the result is fairly consistent: fruit preparations given to diabetic rodents

tend to lower fasting glucose, and some reports describe better lipid profiles as well ([15](#), [16](#), [37](#)). A study of a standardised fruit extract reported effects on glucose and on lipids in diabetic animals and took care to describe the extract, which is exactly the habit the field needs ([15](#)). Comparisons of several Indian plants in alloxan-induced diabetic rats place bitter melon among those with a visible effect, though under conditions that differ from those of streptozotocin work ([37](#)).

What the reports share less is size. Fruit juice, powder, aqueous extract, alcoholic extract and isolated fractions are different materials, and doses are given as weights of fresh fruit, dried powder or extract with no common basis ([12](#), [16](#)). The direction may be reproducible while the magnitude is not.



shading shows how much each kind of evidence can say; schematic, not data

Figure 2. Qualitative map of how much each kind of evidence can say about each question (schematic, not data).

4.2 How the Model Shapes the Result

The features of the model summarised in [Table 3](#) can each move a result without any help from the plant. If glucose is checked only a few days after injection, some animals will still be settling and some will drift back toward normal; if the cut-off for diabetes is generous, mildly affected animals are included who may recover ([25](#), [26](#)). An animal left to settle after the injection behaves differently from one



tested at once. With a partial-loss variant, a plant that merely improves insulin sensitivity can look like a cure.

Table 3. Features of the streptozotocin model that change what a result means.

Feature	Why it matters	Reading consequence
Degree of beta-cell loss	High doses leave little to stimulate (21, 23)	Secretagogue effects hard to see
Partial-loss variants	Closer to type 2 physiology (22, 24)	Insulin-sparing effects testable
Spontaneous recovery	Glucose may drift down untreated (26)	Needs a diabetic control
Strain, sex and diet	Change susceptibility (25, 27)	Limits comparison between papers
Species gap	Rat is not a person (28, 38)	Translation is uncertain

Note: Features are those described in the cited model literature; none is attributed to a single study.

A further matter is whether an observed fall in glucose is specific. Diabetic animals eat and drink more and lose weight, and any treatment that makes them eat less will lower glucose for reasons unrelated to the extract. Pair-fed controls are rarely reported. A fall in glucose that cannot be told apart from the effect of eating less is hard to credit to the extract.

4.3 Quality and Reporting of the Evidence

Many reviews of animal research have found that randomisation, concealed allocation and blinded outcome assessment are described in a minority of papers, and studies that omit them tend to report larger effects (33, 39). Small groups make estimates unstable and exaggerated when they do reach significance (40, 41). Read this way, the absence of an effect in a small study is not evidence of absence. When animals share a cage, the cage and not the animal may be the proper unit of analysis, and ignoring this overstates

precision (34, 35). Negative results are published less often than positive ones, which inflates the apparent success of treatments tested in animals (36). Figure 3 marks where such problems enter a typical study.

None of this is specific to bitter melon, but the plant literature is especially exposed because the test material is itself variable. When the extract is not characterised, another laboratory cannot repeat the work even in principle. The point is not that these studies are poor, only that their results travel less far than their abstracts suggest.

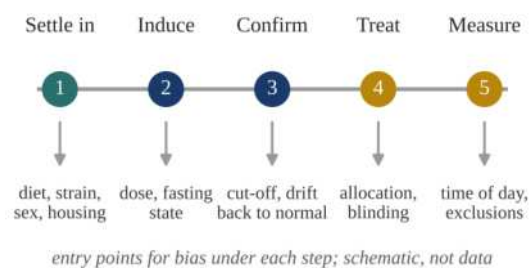


Figure 3. Order of steps in a streptozotocin study and where the main sources of bias enter (schematic, not data).

5. Discussion

5.1 Interpretation

At face value the literature says that bitter melon extracts usually lower glucose in streptozotocin-diabetic rats, that several plausible mechanisms exist, and that people may see a small benefit. Read more carefully, it says that the size of the effect and its mechanism are not settled, that the model can generate apparent benefits through artefacts, and that translation to people is untested at the scale that matters (38, 42, 43). Dose conversion by body surface area is a common approach, but it is only an approximation and cannot make up for an extract of unknown content (44). That is a modest claim, and it is the one the evidence will currently bear. A reader of a rat study needs the answer to a plain



question: would this hold in a person? A positive rat study is a reasonable reason to look further, not a reason to recommend the fruit as a treatment.

5.2 Limitations

The review has limits of its own. It is narrative, the search was not systematic, and the selection of papers depends on the judgement of the authors; a formal systematic review with a protocol would answer questions of effect size that this one cannot. Reviews of this kind are more useful when they say where the evidence stops than when they smooth it over.

5.3 Future Work

A convincing study of a fruit extract in this model would define the extract by part, solvent and a marker, state the model and the cut-off for diabetes, include a diabetic control and a positive control, randomise and blind the work, treat the cage as the unit where animals share one, and report all outcomes including the unfavourable ones (32, 33, 34). Only then would a well-powered trial in people have a firm footing (39). Nothing in this reading argues against studying bitter melon; it argues for measuring carefully what happens when it is given. These points apply with equal force to any herbal extract, not only to bitter melon.

6. Conclusion

Bitter melon is a plausible glucose-lowering plant, and the rat literature points in a consistent direction. What it does not yet give is a reliable estimate of the size of the effect, a confirmed mechanism or a clear link to benefit in people. The streptozotocin model is useful, but its results depend on dose, timing and design choices that are often poorly reported, and the extract itself is rarely defined well enough to be reproduced.

7. Acknowledgements

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9. Conflict of Interest

The authors declare no conflict of interest.

10. Author Contributions

F.M. conceived the review and wrote the sections on the model and its design. D.S. wrote the sections on bitter melon chemistry and mechanisms. W.C. wrote the sections on evidence in people and on reporting quality. All authors revised the manuscript and approved the final version.

11. Ethics Statement

This is a review of published literature. No animals were used and no ethical approval was required.

12. Data Availability

No new data were generated. All sources are cited in the reference list.

13. References

1. Wild, S., Roglic, G., Green, A., Sicree, R., & King, H. (2004). Global prevalence of diabetes: Estimates for the year 2000 and projections for 2030. *Diabetes Care*, 27(5), 1047–1053. DOI: [10.2337/diacare.27.5.1047](https://doi.org/10.2337/diacare.27.5.1047)
2. Guariguata, L., Whiting, D. R., Hambleton, I., Beagley, J., Linnenkamp, U., & Shaw, J. E. (2014). Global estimates of diabetes prevalence for 2013 and projections for 2035. *Diabetes Research and Clinical Practice*, 103(2), 137–149. DOI: [10.1016/j.diabres.2013.11.002](https://doi.org/10.1016/j.diabres.2013.11.002)
3. DeFronzo, R. A. (2009). Banting Lecture. From the triumvirate to the ominous octet: A new paradigm for the treatment of type 2 diabetes mellitus. *Diabetes*, 58(4), 773–795. DOI: [10.2337/db09-9028](https://doi.org/10.2337/db09-9028)
4. Kahn, S. E., Cooper, M. E., & Del Prato, S. (2014). Pathophysiology and treatment of type 2 diabetes: Perspectives on the past, present, and future. *The Lancet*, 383(9922), 1068–1083. DOI: [10.1016/S0140-6736\(14\)60501-X](https://doi.org/10.1016/S0140-6736(14)60501-X)



- [10.1016/S0140-6736\(13\)62154-6](https://doi.org/10.1016/S0140-6736(13)62154-6)
5. Bailey, C. J., & Day, C. (1989). Traditional plant medicines as treatments for diabetes. *Diabetes Care*, 12(8), 553–564. DOI: [10.2337/diacare.12.8.553](https://doi.org/10.2337/diacare.12.8.553)
 6. Marles, R. J., & Farnsworth, N. R. (1995). Antidiabetic plants and their active constituents. *Phytomedicine*, 2(2), 137–189. DOI: [10.1016/S0944-7113\(11\)80059-0](https://doi.org/10.1016/S0944-7113(11)80059-0)
 7. Raman, A., & Lau, C. (1996). Anti-diabetic properties and phytochemistry of *Momordica charantia* L. (Cucurbitaceae). *Phytomedicine*, 2(4), 349–362. DOI: [10.1016/S0944-7113\(96\)80077-X](https://doi.org/10.1016/S0944-7113(96)80077-X)
 8. Grover, J. K., & Yadav, S. P. (2004). Pharmacological actions and potential uses of *Momordica charantia*: A review. *Journal of Ethnopharmacology*, 93(1), 123–132. DOI: [10.1016/j.jep.2004.03.035](https://doi.org/10.1016/j.jep.2004.03.035)
 9. Joseph, B., & Jini, D. (2013). Antidiabetic effects of *Momordica charantia* (bitter melon) and its medicinal potency. *Asian Pacific Journal of Tropical Disease*, 3(2), 93–102. DOI: [10.1016/S2222-1808\(13\)60052-3](https://doi.org/10.1016/S2222-1808(13)60052-3)
 10. Khanna, P., Jain, S. C., Panagariya, A., & Dixit, V. P. (1981). Hypoglycemic activity of polypeptide-p from a plant source. *Journal of Natural Products*, 44(6), 648–655. DOI: [10.1021/np50018a002](https://doi.org/10.1021/np50018a002)
 11. Tan, M. J., Ye, J.-M., Turner, N., Hohnen-Behrens, C., Ke, C.-Q., Tang, C.-P., ... Kraegen, E. W. (2008). Antidiabetic activities of triterpenoids isolated from bitter melon associated with activation of the AMPK pathway. *Chemistry & Biology*, 15(3), 263–273. DOI: [10.1016/j.chembiol.2008.01.013](https://doi.org/10.1016/j.chembiol.2008.01.013)
 12. Harinantenaina, L., Tanaka, M., Takaoka, S., Oda, M., Mogami, O., Uchida, M., & Asakawa, Y. (2006). *Momordica charantia* constituents and antidiabetic screening of the isolated major compounds. *Chemical and Pharmaceutical Bulletin*, 54(7), 1017–1021. DOI: [10.1248/cpb.54.1017](https://doi.org/10.1248/cpb.54.1017)
 13. Basch, E., Gabardi, S., & Ulbricht, C. (2003). Bitter melon (*Momordica charantia*): A review of efficacy and safety. *American Journal of Health-System Pharmacy*, 60(4), 356–359. DOI: [10.1093/ajhp/60.4.356](https://doi.org/10.1093/ajhp/60.4.356)
 14. Yibchok-anun, S., Adisakwattana, S., Yao, C. Y., Sangvanich, P., Roengsumran, S., & Hsu, W. H. (2006). Slow acting protein extract from fruit pulp of *Momordica charantia* with insulin secretagogue and insulinomimetic activities. *Biological and Pharmaceutical Bulletin*, 29(6), 1126–1131. DOI: [10.1248/bpb.29.1126](https://doi.org/10.1248/bpb.29.1126)
 15. Fernandes, N. P. C., Lagishetty, C. V., Panda, V. S., & Naik, S. R. (2007). An experimental evaluation of the antidiabetic and antilipidemic properties of a standardized *Momordica charantia* fruit extract. *BMC Complementary and Alternative Medicine*, 7, 29. DOI: [10.1186/1472-6882-7-29](https://doi.org/10.1186/1472-6882-7-29)
 16. Virdi, J., Sivakami, S., Shahani, S., Suthar, A. C., Banavalikar, M. M., & Biyani, M. K. (2003). Antihyperglycemic effects of three extracts from *Momordica charantia*. *Journal of Ethnopharmacology*, 88(1), 107–111. DOI: [10.1016/S0378-8741\(03\)00182-2](https://doi.org/10.1016/S0378-8741(03)00182-2)
 17. Chen, Q., Chan, L. L. Y., & Li, E. T. S. (2003). Bitter melon (*Momordica charantia*) reduces adiposity, lowers serum insulin and normalizes glucose tolerance in rats fed a high fat diet. *The Journal of Nutrition*, 133(4), 1088–1093. DOI: [10.1093/jn/133.4.1088](https://doi.org/10.1093/jn/133.4.1088)
 18. Shih, C.-C., Lin, C.-H., & Lin, W.-L. (2008). Effects of *Momordica charantia* on insulin resistance and visceral obesity in mice on high-fat diet. *Diabetes Research and Clinical Practice*, 81(2), 134–143. DOI: [10.1016/j.diabres.2008.04.020](https://doi.org/10.1016/j.diabres.2008.04.020)
 19. Chaturvedi, P. (2012). Antidiabetic potentials of *Momordica charantia*: Multiple mechanisms behind the effects. *Journal of Medicinal Food*, 15(2), 101–107. DOI: [10.1089/jmf.2010.0258](https://doi.org/10.1089/jmf.2010.0258)
 20. Leung, L., Birtwhistle, R., Kotecha, J., Hannah, S., & Cuthbertson, S. (2009). Anti-diabetic and hypoglycaemic effects of *Momordica charantia* (bitter melon): A mini review. *British Journal of Nutrition*, 102(12), 1703–1708. DOI: [10.1017/S0007114509992054](https://doi.org/10.1017/S0007114509992054)
 21. Lenzen, S. (2008). The mechanisms of alloxan- and streptozotocin-induced diabetes. *Diabetologia*, 51(2), 216–226. DOI: [10.1007/s00125-007-0886-7](https://doi.org/10.1007/s00125-007-0886-7)
 22. Srinivasan, K., Viswanad, B., Asrat, L., Kaul, C. L., & Ramarao, P. (2005). Combination of high-fat diet-fed and low-dose streptozotocin-treated rat: A model for type 2 diabetes and pharmacological screening. *Pharmacological Research*, 52(4), 313–320. DOI: [10.1016/j.phrs.2005.05.004](https://doi.org/10.1016/j.phrs.2005.05.004)
 23. Masiello, P., Broca, C., Gross, R., Roye, M., Manteghetti, M., Hillaire-Buys, D., ... Ribes, G. (1998). Experimental NIDDM: Development of a new model in adult rats administered streptozotocin and nicotinamide. *Diabetes*, 47(2), 224–229. DOI: [10.2337/diab.47.2.224](https://doi.org/10.2337/diab.47.2.224)
 24. Ghasemi, A., Khalifi, S., & Jedi, S. (2014). Streptozotocin-nicotinamide-induced rat model of type 2 diabetes. *Acta Physiologica Hungarica*, 101(4), 408–420. DOI: [10.1556/APhysiol.101.2014.4.2](https://doi.org/10.1556/APhysiol.101.2014.4.2)
 25. Furman, B. L. (2015). Streptozotocin-induced diabetic models in mice and rats. *Current Protocols in Pharmacology*, 70, 5.47.1–5.47.20. DOI: [10.1002/0471141755.ph0547s70](https://doi.org/10.1002/0471141755.ph0547s70)



26. Deeds, M. C., Anderson, J. M., Armstrong, A. S., Gastineau, D. A., Hiddinga, H. J., Jahangir, A., ... Kudva, Y. C. (2011). Single dose streptozotocin-induced diabetes: Considerations for study design in islet transplantation models. *Laboratory Animals*, 45(3), 131–140. DOI: [10.1258/la.2010.010090](https://doi.org/10.1258/la.2010.010090)
27. King, A. J. F. (2012). The use of animal models in diabetes research. *British Journal of Pharmacology*, 166(3), 877–894. DOI: [10.1111/j.1476-5381.2012.01911.x](https://doi.org/10.1111/j.1476-5381.2012.01911.x)
28. Rees, D. A., & Alcolado, J. C. (2005). Animal models of diabetes mellitus. *Diabetic Medicine*, 22(4), 359–370. DOI: [10.1111/j.1464-5491.2005.01499.x](https://doi.org/10.1111/j.1464-5491.2005.01499.x)
29. Ooi, C. P., Yassin, Z., & Hamid, T. A. (2012). *Momordica charantia* for type 2 diabetes mellitus. *Cochrane Database of Systematic Reviews*, (8), CD007845. DOI: [10.1002/14651858.CD007845.pub3](https://doi.org/10.1002/14651858.CD007845.pub3)
30. Fuangchan, A., Sonthisombat, P., Seubnukarn, T., Chanouan, R., Chotchaisuwongse, P., Thaneerat, T., ... Pongpeerapat, A. (2011). Hypoglycemic effect of bitter melon compared with metformin in newly diagnosed type 2 diabetes patients. *Journal of Ethnopharmacology*, 134(2), 422–428. DOI: [10.1016/j.jep.2010.12.045](https://doi.org/10.1016/j.jep.2010.12.045)
31. Krawinkel, M. B., & Keding, G. B. (2006). Bitter gourd (*Momordica charantia*): A dietary approach to hyperglycemia. *Nutrition Reviews*, 64(7), 331–337. DOI: [10.1111/j.1753-4887.2006.tb00219.x](https://doi.org/10.1111/j.1753-4887.2006.tb00219.x)
32. Kilkenney, C., Browne, W. J., Cuthill, I. C., Emerson, M., & Altman, D. G. (2010). Improving bioscience research reporting: The ARRIVE guidelines for reporting animal research. *PLoS Biology*, 8(6), e1000412. DOI: [10.1371/journal.pbio.1000412](https://doi.org/10.1371/journal.pbio.1000412)
33. Hooijmans, C. R., Rovers, M. M., de Vries, R. B. M., Leenaars, M., Ritskes-Hoitinga, M., & Langendam, M. W. (2014). SYRCLE's risk of bias tool for animal studies. *BMC Medical Research Methodology*, 14, 43. DOI: [10.1186/1471-2288-14-43](https://doi.org/10.1186/1471-2288-14-43)
34. Festing, M. F. W., & Altman, D. G. (2002). Guidelines for the design and statistical analysis of experiments using laboratory animals. *ILAR Journal*, 43(4), 244–258. DOI: [10.1093/ilar.43.4.244](https://doi.org/10.1093/ilar.43.4.244)
35. Hurlbert, S. H. (1984). Pseudoreplication and the design of ecological field experiments. *Ecological Monographs*, 54(2), 187–211. DOI: [10.2307/1942661](https://doi.org/10.2307/1942661)
36. Sena, E. S., van der Worp, H. B., Bath, P. M. W., Howells, D. W., & Macleod, M. R. (2010). Publication bias in reports of animal stroke studies leads to major overstatement of efficacy. *PLoS Biology*, 8(3), e1000344. DOI: [10.1371/journal.pbio.1000344](https://doi.org/10.1371/journal.pbio.1000344)
37. Kar, A., Choudhary, B. K., & Bandyopadhyay, N. G. (2003). Comparative evaluation of hypoglycaemic activity of some Indian medicinal plants in alloxan diabetic rats. *Journal of Ethnopharmacology*, 84(1), 105–108. DOI: [10.1016/S0378-8741\(02\)00144-7](https://doi.org/10.1016/S0378-8741(02)00144-7)
38. Cefalu, W. T. (2006). Animal models of type 2 diabetes: Clinical presentation and pathophysiological relevance to the human condition. *ILAR Journal*, 47(3), 186–198. DOI: [10.1093/ilar.47.3.186](https://doi.org/10.1093/ilar.47.3.186)
39. Hooijmans, C. R., & Ritskes-Hoitinga, M. (2013). Progress in using systematic reviews of animal studies to improve translational research. *PLoS Medicine*, 10(7), e1001482. DOI: [10.1371/journal.pmed.1001482](https://doi.org/10.1371/journal.pmed.1001482)
40. Button, K. S., Ioannidis, J. P. A., Mokrysz, C., Nosek, B. A., Flint, J., Robinson, E. S. J., & Munafò, M. R. (2013). Power failure: Why small sample size undermines the reliability of neuroscience. *Nature Reviews Neuroscience*, 14(5), 365–376. DOI: [10.1038/nrn3475](https://doi.org/10.1038/nrn3475)
41. Ioannidis, J. P. A. (2005). Why most published research findings are false. *PLoS Medicine*, 2(8), e124. DOI: [10.1371/journal.pmed.0020124](https://doi.org/10.1371/journal.pmed.0020124)
42. Perel, P., Roberts, I., Sena, E., Wheble, P., Briscoe, C., Sandercock, P., ... Khan, K. S. (2007). Comparison of treatment effects between animal experiments and clinical trials: Systematic review. *BMJ*, 334(7586), 197. DOI: [10.1136/bmj.39048.407928.BE](https://doi.org/10.1136/bmj.39048.407928.BE)
43. Hackam, D. G., & Redelmeier, D. A. (2006). Translation of research evidence from animals to humans. *JAMA*, 296(14), 1731–1732. DOI: [10.1001/jama.296.14.1731](https://doi.org/10.1001/jama.296.14.1731)
44. Reagan-Shaw, S., Nihal, M., & Ahmad, N. (2008). Dose translation from animal to human studies revisited. *The FASEB Journal*, 22(3), 659–661. DOI: [10.1096/fj.07-9574LSF](https://doi.org/10.1096/fj.07-9574LSF)