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A Review on Futuristic Scope of Agents Related to Amphibian's Skin and Plants-based Sources in Type 2 Antidiabetic Therapies

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Abstract

Based on the current scenario type-2 diabetes has been labelled as one of the major health issues, approaching exponentially towards mind boggling stage of epidemic globally. Considering to its lifelong latency from early to old ages, less awareness to its particular genotype and phenotype and hefty cost involved in its management and treatment; there is substantial need for more advance, personalised and economical therapeutic approaches for its effective therapy and treatment. The current review here discusses peculiar agents from amphibian's skin and rarely explored distinctive plant sources with potential to be a viable therapeutic option for type-2 diabetes, therefore, could be devised into effective future treatment strategy to it and also to its related microvascular and macrovascular complications. Based on the literature search the therapeutic scope of agents from amphibian's skin and selected plants sources are delineated, sighting their activities and prospects as to be future revolutionary remedy to type-2 diabetes and associated hitches such as their insulin releasing ability in pancreatic beta cell lines and primary islets cells, effects on glucose level and on other metabolic parameters such as obesity, lipid profile and pancreatic beta cell function etc.

Keywords: Type-2 diabetes, Distinctive plant sources, Metabolic parameters, Glucose level, Peculiar agents and amphibian's skin.

INTRODUCTION

Type 2 diabetes also refer as to noninsulin dependent diabetes mellitus is a chronic metabolic disorder characterized by hyperglycemia as result of insufficient insulin secretion by pancreatic beta cells/inability of tissues to respond to biological action of released insulin or both. This prolonged, elevated glucose level further observed to add up multiple microvascular and macrovascular complications in type 2 diabetes patients.[1,2]

The prevalence of diabetes around the world is increasing exponentially despite of rigorous research and discovery multiple antidiabetic agents both conventional and non-conventional. As per recent stats, number of individuals affected with diabetes in 1980 rose from 108 million to 422 million in year 2014 globally and are expected to rise to 642 million by 2040. Moreover, diabetes being a major cause to diseases like heart attack, blindness, kidney failure etc has been directly associated to 1.6 million deaths and 2.2 million deaths were recorded due to its major complications such as rise in glucose level in year 2015.

In specific to UK, in year 2019 almost 4.7 million of people has been diagnosed with diabetes i.e. 1 in every 10 individual and the number of people are thought to ascend to 5.5 million by 2030(6% of UK population). Similarly, in country like India a developing nation hold one of the largest diabetic population of 69 million and by 2030, these Figures are estimated to grow up to 109 million, thus, projecting diabetes as the global health issue and a major burden to number of countries economies.[3-6]

Considering such staggering incidence rates and limitations concerning to currently available antidiabetic agents, there is an urgent need to more economical and novel treatment strategies with minimal side effects. Therefore, owing to the vast applications and important sources from nature in the field of medical sciences, developing bio prospected amphibian skin and plant based bioactive compounds might turn to novel method devising a therapeutically effective treatment options for type 2 diabetes and possibility of creating steadfast health care solutions in the respected field.[7-12]

At present, evidence suggest both amphibians' skin/plant-based treatments could be adopted as future frontline approaches to diabetes therapy. Research shows that peptides from variety of frog skin sources hold immense potential to be developed into anti diabetic agents. Host defense peptides and their derived analogues from amphibian sources like Esculentin-2Cha,[13-16] Tigerinin-1R,[17-20] PGLa-AM1,[11,21] Hymenochirin-1b,[22-24] Brevinin,[25-27] Magainin-AM2,[28,29] Xenopsin,[30-32] Careulein,[33] Temporin,[34] Alyteserin,[35] Gaegurin-6,[36] CPF-SE1,[37] etc. has been observed to exhibit overwhelming insulinotropic/ Glucoregulatory effects via improving beta/islet cell function, glucose tolerance/homeostasis, *in vitro* stimulation to insulin release/sensitivity, glycaemic control and secretion of glucagon-like peptide 1 (GLP-1) in high fed obese animal models. Moreover, they have also been witnessed to cause significant reduction to pancreatic insulin, plasma glucagon concentrations and total body fat and plasma triglyceride levels.

Similarly, extracts/agents from multiple plant species like *Humulus lupulus,*[38] *Medicago sativa*,[39-41] *Agrimony eupatoria*,[42] *Ocimum sanctum*,[43,44] *Cinnamomum*

zeylanicum,[45-47] Terminalia *bellirica,*[48] *Asparagus racemosus*,[49] *Terminalia chebula*,[50,51] *Asparagus adscendens*,[52,53] *Curcuma longa*,[54,55] *Swertiya chirayita,*[56] *Trigonella foenum-grecum*,[57,58] etc also carry's prospects to be developed into vital anti diabetic agents. Additionally, the drug Metformin widely used in modern era in diabetes is also derived from plant *Galega officinalis*.[59]

However, decades of research on variety of such amphibian's skin/ plants-based agents none of the steadfast and economical solutions has been achieved till date countering type 2 form of diabetes and its related complications. Based on this fact the current review here aims to discuss unique and less widely explored agents from natural sources like insulinotropic peptides isolated from frog skin secretions belonging to class Pipidae and agents from marine/local plants *(Laguncularia racemosa*, *Pterocarpus marsupium* and *Cymodocea nodosa)* bearing immense potential to be transformed into vital futuristic therapy against type-2 Diabetes.

The profiling of the agents will be done based on their past and current research abilities against diabetes and related complications such as their insulin releasing ability in cell lines like BRIN-BD11 beta pancreatic cell lines (*in vitro*) and also in obese diabetic animal models (*in-vivo*) concerning to their potency to regulate glucose-tolerance and facilitating insulin-release etc.

Frog Skin Based Peptides

In the search of viable and steadfast effective health solutions against serious diseases and infections in the field of medical sciences, host defense peptides isolated from frog skin could be major breakthrough laying down effective future therapeutic options. There have been number of proofs suggesting peptides isolated from frog skin showing diverse therapeutic abilities such as cytolytic activities against variety of bacteria and fungi, as to their designated activity to function as host defense peptides against pathogenic microbes.[60-63] Moreover, evidences propose that the isolated peptides also holds potential to be an vital anticancer/antitumor,[64-67] antiviral,[68-70] immunomodulatory,[71,72] agents etc.[10]

Similarly, regarding effective antidiabetic activities, peptide isolated from Pipdae family frogs hold immense ability to be developed into as conventional diabetic therapy.

Members belonging to Pipidae family also known as to be the clawed frogs, identified with their dorsoventral flattened body. They are further divided mainly into four genera based on their geographical existence. The very first South American native Pipa while the other four *Pseudhymenochirus*, *Xenopus, Hymenochirus, Silurana are* found in sub-Saharan Africa. Moreover, having taxonomically dubious evolutionary history, some frogs of the family such as S*ilurana* and *Xenopus* are also subclassed *in* Xenopodinae family.[11,73-76]

Insulinotropic peptides from Pipdae family

The skin secretion from this frog family contains multiple numbers of peptides out of which few have shown prospects to developed into antidiabetic agents.

Peptides from *Xenopus amieti*: The skin secretions from *Xenopus amieti* an octoploid volcano clawed frog carry's diverse range of peptides:

Magainin (AM1 and AM2): Based on the immense potential, both Magainin AM1 and Magainin AM2 have been observed with antidiabetic activities at both *in-vitro* (clonal BRINB11 β-cells) and *in-vivo* (mouse islets) levels. Magainin-AM1 at ≥ 100nM concentration has been witnessed to show nontoxic concentration dependent facilitation of insulin release in clonal BRINB11 β-cells cell lines and isolated mouse islets. However, Magainin-AM2 was found to be more potent to stimulate insulin release from clonal BRINB11 β-cells cell lines and in mouse islets along with improving glucose tolerance and consistent reduction in non-fasting blood glucose level and upregulation of non-fasting plasma insulin concentration thus, maintaining glucose homeostatis and beta cell function in high fed obese mice. Moreover, they have also been found to stimulate rate of release of glucagon like peptides (GLP-1) and incretin peptides in murine enteroendocrine GLUTag cell lines at non pernicious concentrations to cells and were also significantly able to induce membrane depolarization and intracellular Calcium (Ca^{2+}) in BRIN –BD11 cell lines.[11,28,77]

Similarly other peptides from *Xenopus amieti* like PGLa-AM1, Xenopsin-precursor fragment (XPF-AM1), Caerulin precursor Fragments (CPF-AM1, AM2, AM3 and AM4) had also shown decisive action to produce significant induction of insulin release in BRIN-BD11 cell lines, mouse islets and human based pancreatic β-cell lines 1.1 B4 at appropriate concentration without any toxicity to the cells.[77]

Peptides from *Hymenochirus boettgeri*: The skin secretions from *Hymenochirus boettgeri* an Congo dwarf clawed frog contains peptides with almost similar structures known as to be hymenochyrins,[78,79] out of which Hymenochirin-1B(a cationic, amphipathic, α-helical peptide) and its related analogues has been observed with the ability to increase the rate of concentration dependent insulin in BRIN-BD11 cells with no cell toxicity at adequate concentration and in mouse islets. The related peptides [P5K] and [D9K], based on their structural activities displayed maximum insulin release rate in mouse islets which was more than to its native peptide. Additionally, there, intraperitoneal administration to high fed obese mice has resulted into improved glucose tolerance along with the up regulated insulin secretions.[22-23,77] Moreover, peptides from this frog skin secretion have also been witnessed to show immunomodulatory, antibacterial, anti-tumor activities.[80,81]

Peptide from *Pseudhymenochirus merlini*: *Pseudhymenochirus merlini* also known as to be Merlin's clawed frog, their skin secretions similar to other pipidae frogs in the family carry's number of cationic, α-helical host-defense peptides like Pseudhymenochirin–1 Pa and −1Pb almost resembling to each other except by one amino acid as well as hymenochirin peptide,[82] while the other peptide pseudhymenochirin–2 Pa peptide doesn't resemble to any of the peptide in the family pepidae. It has been witnessed that pseudhymenochirin-1Pb and pseudhymenochirin–2 Pa both the peptides were able to induce insulin release in BRINBD11 clonal beta cells at certain concentrations. Additionally analogues [R8r] of pseudhymenochirin-1Pb also found to potentiate insulin release with low hemolytic activity. Additionally, along with insulinotropic acitvities the peptides from this frog were also been found to show effective antimicrobial activity with broad spectrum along with antitumor activity in mammalian cells.[24,77]

Plant based agents with medicinal properties

There have been numbers of plant-based agents that has been utilized to elicit medicinal responses to variety of diseases including those whose etiology and occurrence is still needed to be addressed immensely. Plant based agents such as Curcumin, Resveratrol, Epigallocatechin-3-gallate (EGCG) etc,[83-85] has been witnessed to show anticancer ability while there are several other plant agents with variety of medicinal activities like antimicrobial,[86,87] antiviral,[88,89] and antidepressant,[90,91] antioxidant activities, antitumor, antifungal etc.[92,93] However, keeping in mind the multi-application use of plant based agents

none of the permanent solution has been achieved till date especially to those diseases which are still conundrum for the researcher around the world like HIV, Cancer, and Diabetes etc.

Therefore, to achieve steadfast solutions for diseases like diabetes exploring unique plant sources and related agents which has not been studied or little has been discovered about their biological activity could be novel way for achieving therapeutic advancement in drug therapy.

Antidiabetic/Insulinotropic activity of prospected plant-based agents

As to device futuristic antidiabetic drugs the review here explores the biological activity of unique marine plant *Laguncularia racemosa* along with *Pterocarpus marsupium* and their possibility to be the developed into advance antidiabetic therapy. The profiling to their prospects to be developed as antidiabetic/insulinotropic agent is done based on their previous biological and antidiabetic-activity if any.

***Laguncularia racemosa*:** Being unique and less widely explored marine plant *Laguncularia racemosa* is rarely been reported for its antidiabetic activity. However, its hydroalcholic and methanolic extracts has been witnessed to show enzymatic activity and thrombin-induced plasma coagulation.[94] Moreover, the ethyl-acetate extracts of endophytic-fungi strains obtained from their leaves has shown potent antimicrobial-activities towards. bacteria like *Staphylococcus aureus, Escherichia coli, Pseudumonas aeruginosa* etc.in addition to its phenolic. compound integracin with protein. kinase inhibitotry activity in suppression of variety of human tumour.[95-97]

***Pterocarpus marsupium*:** The Phenolic/aqueous extract from the leaves/roots of *Pterocarpus marsupium* has shown to be capable of managing hyperglycemia, hyperlipidemia and major diabetes related-complications through reduction of fasting blood-glucose level, glycosylated haemoglobin levels and facilitating the serum insulin and glycogen-contents to skeletal&hepatic-muscle.in diabetic-rats.[98-104] While its crude and stem bark extracts were also found to possess anti hyperglycaemic activity with ability to lower elevated glucose in animal-models.[105,107] Moreover, the methanolic/aqueous extract of stem bark.

***Cymodocea nodosa*:** Similar to *Laguncularia racemosa*, *Cymodocea nodosa* is also a Marine plant, which has been not been so much explored in regards to its biological activities. However, it extracts in recent research has shown to be a very effective in diabetes treatment and its related complications. The extracts from plant have been observed to inhibit vital hypelglycaemia inducing enzyme and α-amylase activity, shielding the pancreatic beta cells and its function thus, decreasing glucose level in blood and regulating lipid levels in alloxan-induced diabetic rat. Moreover, the extract has also shown to reduce the body weight while inhibiting the lipase activity in obese high fed rats leading to decreased triglycerides levels, low density lipoproteins (LDL), total cholesterol level and rise in high density lipoprotein cholesterol (HDL) and maintaining blood lipid homeostasis.[108-110]

CONCLUSION

The scope of bioactive peptides/agents from unique natural sources such as rare species of plants or amphibian's skins sources as enduring therapeutic option for diabetes is very much of interest and new direction for researchers around the world in terms to their distinctive attributes and functional features. Considering the fact based on the limitations to currently available conventional diabetes medications there is a stern and immediate need to explore such novel agents/peptides that has rarely been studied for their biological activity and therefore could be potentially devised into a futuristic anti diabetic therapy. Diabetes based on its long latency, which not only have negative health effects on patients but also have consistent mental and financial impact. As also being common, with staggering number of increasing incidence rates around the world diabetes is an ideal choice for research and is also comparatively easy to monitor as other diseases. The Preliminary data presented in the review shows the substantial prospective for the peptides/agents and their potential activity against diabetes and its related complications. However, such interventions through rare biological source of means could be time consuming and require multiple phases of clinical study done meticulously before can be recommended to as useful anti diabetic treatment strategies for patients. Thus, a confirmational activity for peptides/agents along with their optimal doses, usage, administration profiling etc are very much desirable through a well-designed clinical trial.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

REFERENCES

1. American Diabetes Association. American Diabetes Association. 2. Classification and diagnosis of diabetes: Standards of medical care in Diabetes-2020. Diabetes Care. 2020 Jan;43(Suppl 1);Suppl 1:S14-31. doi: 10.2337/dc20-S002, PMID 31862745.
2. Yonel Z, Batt J, Jane R, Cerullo E, Gray LJ, Dietrich T *et al*. The role of the oral healthcare team in identification of type 2 diabetes mellitus: A systematic review. Curr Oral Health Rep. 2020;7(1):87-97. doi: 10.1007/s40496-020-00250-w.
3. World Health Organization (WHO). Diabetes(statistics); 2017. Available from: http://www.who.int/mediacentre/factsheets/fs312/en/.Accessed-Mar-10th-2020 [cited 9/13/2022].
4. Walker JD, Slater M, Jones CR, Shah BR, Frymire E, Khan S, *et al*. Diabetes prevalence, incidence and mortality in First Nations and other people in Ontario, 1995-2014: A population-based study using linked administrative data. CMAJ. 2020;192(6):E128-35. doi: 10.1503/cmaj.190836, PMID 32041696.
5. Diabetes UK. Too of ten missing: Making emotional and psychological support routine in diabetes care. London: Diabetes UK; 2020.
6. Diabetes UK. Diabetes prevalence. Vol. 2020; 2019.
7. Parim B, Sathibabu Uddandrao VV, Saravanan G. Diabetic cardiomyopathy: Molecular mechanisms, detrimental effects of conventional treatment, and beneficial effects of natural therapy. Heart Fail Rev. 2019;24(2):279-99. doi: 10.1007/s10741-018-9749-1, PMID 30349977.
8. Hoda M, Hemaiswarya S, Doble M. Polyphenol nanoformulations with potential antidiabetic properties. Inrole of Phenolic Phytochemicals in Diabetes Management 2019 (pp. 145-57). Berlin: Springer.
9. Aryaeian N, Sedehi SK, Arablou T. Polyphenols and their effects on diabetes management: A review. Med J Islam Repub Iran. 2017;31:134. doi: 10.14196/mjiri.31.134, PMID 29951434.
10. Conlon JM, Mechkarska M, Lukic ML, Flatt PR. Potential therapeutic applications of multifunctional host-defense peptides from frog skin as anti-cancer, anti-viral, immunomodulatory, and anti-diabetic agents. Peptides. 2014;57:67-77. doi: 10.1016/j.peptides.2014.04.019, PMID 24793775.
11. Ojo OO, Conlon JM, Flatt PR, Abdel-Wahab YH. Frog skin peptides (tigerinin-1R, magainin-AM1,-AM2, CPF-AM1, and PGla-AM1) stimulate secretion of glucagon-like peptide 1 (GLP-1) by GLUTag cells. Biochem Biophys Res Commun. 2013;431(1):14-8. doi: 10.1016/j.bbrc.2012.12.116, PMID 23291176.
12. Marenah L, Flatt PR, Orr DF, McClean S, Shaw C, Abdel-Wahab YH. Skin secretion of the toad *Bombina variegata* contains multiple insulin-releasing peptides including bombesin and entirely novel insulinotropic structures. Biol Chem. 2004;385(3-4):315-21. doi: 10.1515/BC.2004.027, PMID 15134346.
13. Vasu S, Ojo OO, Moffett RC, Conlon JM, Flatt PR, Abdel-Wahab YHA. Anti-diabetic actions of esculentin-2CHa (1-30) and its stable analogues in a diet-induced model of obesity-diabetes. Amino Acids. 2017;49(10):1705-17. doi: 10.1007/s00726-017-2469-3, PMID 28836148.
14. Vasu S, McGahon MK, Moffett RC, Curtis TM, Conlon JM, Abdel-Wahab YH *et al*. Esculentin-2CHa (1-30) and its analogues: Stability and mechanisms of insulinotropic action. J Endocrinol. 2017;232(3):423-35. doi: 10.1530/JOE-16-

0453, PMID 28115493.

15. Abdel-Wahab Y, Flatt P, Ojo O, Conlon JM, inventors. Esculentin-2CHa peptide and analogues thereof. United States patent US. 2019;10(202):427.
16. Ojo OO, Srinivasan DK, Owolabi BO, Vasu S, Conlon JM, Flatt PR *et al*. Esculentin-2CHa-related peptides modulate islet cell function and improve glucose tolerance in mice with diet-induced obesity and insulin resistance. PLOS ONE. 2015 Oct 29;10(10):e0141549. doi: 10.1371/journal.pone.0141549, PMID 26512980.
17. Ojo OO, Srinivasan DK, Owolabi BO, McGahon MK, Moffett RC, Curtis TM *et al*. Molecular mechanisms mediating the beneficial metabolic effects of [Arg4] tigerinin-1R in mice with diet-induced obesity and insulin resistance. Biol Chem. 2016 Aug 1;397(8):753-64. doi: 10.1515/hsz-2016-0120, PMID 26966929.
18. Ojo OO, Srinivasan DK, Owolabi BO, Flatt PR, Abdel-Wahab YH. Beneficial effects of tigerinin-1R on glucose homeostasis and beta cell function in mice with diet-induced obesity-diabetes. Biochimie. 2015;109:18-26. doi: 10.1016/j.biochi.2014.11.018, PMID 25483926.
19. Srinivasan D, Ojo OO, Abdel-Wahab YH, Flatt PR, Guilhaudis L, Conlon JM. Insulin-releasing and cytotoxic properties of the frog skin peptide, tigerinin-1R: A structure–activity study. Peptides. 2014;55:23-31. doi: 10.1016/j.peptides.2014.02.002, PMID 24530698.
20. Ojo OO, Abdel□Wahab YH, Flatt PR, Mechkarska M, Conlon JM. Tigerinin□1R: A potent, non□toxic insulin□releasing peptide isolated from the skin of the Asian frog, Hoplobatrachus rugulosus. Diabetes Obes Metab. 2011;13(12):1114-22. doi: 10.1111/j.1463-1326.2011.01470.x, PMID 21736689.
21. Owolabi BO, Musale V, Ojo OO, Moffett RC, McGahon MK, Curtis TM *et al*. Actions of PGLa-AM1 and its [A14K] and [A20K] analogues and their therapeutic potential as anti-diabetic agents. Biochimie. 2017;138:1-12. doi: 10.1016/j.biochi.2017.04.004, PMID 28392407.
22. Owolabi BO, Ojo OO, Srinivasan DK, Conlon JM, Flatt PR, Abdel-Wahab YH. *In vitro* and *in vivo* insulinotropic properties of the multifunctional frog skin peptide hymenochirin-1B: A structure–activity study. Amino Acids. 2016;48(2):535-47. doi: 10.1007/s00726-015-2107-x, PMID 26439377.
23. Owolabi BO, Ojo OO, Srinivasan DK, Conlon JM, Flatt PR, Abdel-Wahab YH. Glucoregulatory, endocrine and morphological effects of [P5K] hymenochirin-1B in mice with diet-induced glucose intolerance and insulin resistance. Naunyn Schmiedebergs Arch Pharmacol. 2016;389(7):769-81. doi: 10.1007/s00210-016-1243-5, PMID 27068334.
24. Manzo G, Scorciapino MA, Srinivasan D, Attoub S, Mangoni ML, Rinaldi AC *et al*. Conformational Analysis of the Host-Defense Peptides Pseudhymenochirin-1Pb and -2Pa and Design of Analogues with Insulin-Releasing Activities and Reduced Toxicities. J Nat Prod. 2015;78(12):3041-8. doi: 10.1021/acs.jnatprod.5b00843, PMID 26606380.
25. Abdel-Wahab YHA, Patterson S, Flatt PR, Conlon JM. Brevinin-2-related peptide and its [D4K] analogue stimulate insulin release *in vitro* and improve glucose tolerance in mice fed a high fat diet. Horm Metab Res. 2010;42(9):652-6. doi: 10.1055/s-0030-1254126.
26. Marenah L, Flatt PR, Orr DF, Shaw C, Abdel-Wahab YH. Skin secretions of *Rana saharica* frogs reveal antimicrobial peptides esculentins-1 and -1B and brevinins-1E and -2EC with novel insulin releasing activity. J Endocrinol. 2006;188(1):1-9. doi: 10.1677/joe.1.06293, PMID 16394170.
27. Marenah L, Flatt PR, Orr DF, McClean S, Shaw C, Abdel-Wahab YH. Brevinin-1 and multiple insulin-releasing peptides in the skin of the frog *Rana palustris*. J Endocrinol. 2004;181(2):347-54. doi: 10.1677/joe.0.1810347, PMID 15128283.
28. Ojo OO, Srinivasan DK, Owolabi BO, Conlon JM, Flatt PR, Abdel-Wahab YH. Magainin-AM2 improves glucose homeostasis and beta cell function in high-fat fed mice. Biochim Biophys Acta. 2015;1850(1):80-7. doi: 10.1016/j.bbagen.2014.10.011, PMID 25459513.
29. Ojo O, Srinivasan D, Owolabi B, Flatt P, Abdel-Wahab Y. Magainin-related peptides stimulate insulin-release and improve glucose tolerance in high fat fed mice. Protein Pept Lett. 2015;22(3):256-63. doi: 10.2174/0929866521666141229105757.
30. Conlon JM, Mechkarska M, Kolodziejek J, Leprince J, Coquet L, Jouenne T *et al*., hosts. Host-Defense and trefoil factor family peptides in skin secretions of the Mawa clawed frog *Xenopus boumbaensis* (Pipidae). Peptides. 2015;72:44-9. doi: 10.1016/j.peptides.2015.03.025, PMID 25849343.
31. Zahid OK, Mechkarska M, Ojo OO, Abdel-Wahab YH, Flatt PR, Meetani MA *et al*. Caerulein-and xenopsin-related peptides with insulin-releasing activities from skin secretions of the clawed frogs, *Xenopus borealis* and *Xenopus amieti* (Pipidae). Gen Comp Endocrinol. 2011;172(2):314-20. doi: 10.1016/j.ygcen.2011.03.022, PMID 21458457.
32. Ojo OO, Flatt PR, Abdel-Wahab YH, Conlon JM. Insulin-releasing peptides. Handbook of biologically Active Peptides. Amsterdam: Elsevier; 2013.
33. Srinivasan D, Mechkarska M, Abdel-Wahab YH, Flatt PR, Conlon JM. Caerulein precursor fragment (CPF) peptides from the skin secretions of *Xenopus laevis* and *Silurana epitropicalis* are potent insulin-releasing agents. Biochimie. 2013;95(2):429-35. doi: 10.1016/j.biochi.2012.10.026, PMID 23142129.
34. Abdel-Wahab YH, Marenah L, Flatt PR, Conlon JM. Insulin releasing properties of the temporin family of antimicrobial peptides. Protein Pept Lett. 2007;14(7):702-7. doi: 10.2174/092986607781483822, PMID 17897097.
35. Ojo OO, Abdel-Wahab YH, Flatt PR, Conlon JM. Insulinotropic actions of the frog skin host-defense peptide alyteserin-2a: A structure-activity study Host-Defense Peptide Alyteserin□2a: A Structure–Activity Study. Chem Biol Drug Des. 2013;82(2):196-204. doi: 10.1111/cbdd.12151, PMID 23742240.
36. Kim JH, Lee JO, Jung JH, Lee SK, You GY, Park SH *et al*. Gaegurin-6 stimulates insulin secretion through calcium influx in pancreatic β Rin5mf cells. Regul Pept. 2010;159(1-3):123-8. doi: 10.1016/j.regpep.2009.07.014, PMID 19651162.
37. Srinivasan D, Ojo OO, Owolabi BO, Conlon JM, Flatt PR, Abdel-Wahab YHA. The frog skin host-defense peptide CPF-SE1 improves glucose tolerance, insulin sensitivity and islet function and decreases plasma lipids in high-fat fed mice. Eur J Pharmacol. 2015;764:38-47. doi: 10.1016/j.ejphar.2015.06.042, PMID 26123844.
38. Takahashi K, Osada K. Effect of dietary purified xanthohumol from hop (*Humulus lupulus* L.) pomace on adipose tissue mass, fasting blood glucose level, and lipid metabolism in KK-Ay mice. J Oleo Sci. 2017;66(5):531-41. doi: 10.5650/jos.ess16234, PMID 28413193.
39. Farsani MK, Amraie E, Kavian P, Keshvari M. Effects of aqueous extract of alfalfa on hyperglycemia and dyslipidemia in alloxan-induced diabetic Wistar rats. Interv Med Appl Sci. 2016;8(3):103-8. doi: 10.1556/1646.8.2016.3.5, PMID 28203391.
40. Seida A, El-Hefnawy H, Abou-Hussein D, Mokhtar FA, Abdel-Naim A. Evaluation of *Medicago sativa* L. sprouts as antihyperlipidemic and antihyperglycemic agent. Pak J Pharm Sci. 2015;28(6):2061-74. PMID 26639479.
41. Öztürk Y, Öztürk N. Plant- and nutraceutical-based approach for the management of diabetes and its neurological complications: A narrative review. Curr Pharm Des. 2019;25(33):3536-49. doi: 10.2174/1381612825666191014165633, PMID 31612820.
42. Ivanova D, Vankova D, Nashar M. *Agrimonia eupatoria* tea consumption in relation to markers of inflammation, oxidative status and lipid metabolism in healthy subjects. Arch Physiol Biochem. 2013;119(1):32-7. doi: 10.3109/13813455.2012.729844, PMID 23078582.
43. Hannan J, Ojo O, Rokeya L, Khaleque J, Akhter M, Flatt P *et al*. Actions underlying antidiabetic effects of *Ocimum sanctum* leaf extracts in animal models of type 1 and type 2 diabetes. Eur J Med Plants. 2015;5(1):1-12. doi: 10.9734/EJMP/2015/11840.
44. Hannan JM, Marenah L, Ali L, Rokeya B, Flatt PR, Abdel-Wahab YH. *Ocimum sanctum* leaf extracts stimulate insulin secretion from perfused pancreas, isolated islets and clonal pancreatic β-cells. J Endocrinol. 2006;189(1):127-36. doi: 10.1677/joe.1.06615, PMID 16614387.
45. Sharma S, Mishra V, Srivastava N. Protective effect of *Trigonella foenum-Graecum* and *Cinnamomum zeylanicum* against diabetes induced oxidative DNA damage in rats. Indian J Biochem Biophys (IJBB). 2020;57(1):15-26.
46. Jain S, Sangma T, Shukla SK, Mediratta PK. Effect of *Cinnamomum zeylanicum* extract on scopolamine-induced cognitive impairment and oxidative stress in rats. Nutr Neurosci. 2015;18(5):210-6. doi: 10.1179/1476830514Y.0000000113, PMID 24559058.
47. Sharafeldin K, Rizvi MR. Effect of traditional plant medicines (*Cinnamomum zeylanicum* and *Syzygium cumini*) on oxidative stress and insulin resistance in streptozotocin-induced diabetic rats. J Basic Appl Zool. 2015;72:126-34. doi: 10.1016/j.jobaz.2015.09.002.
48. Uddin SJ, Afroz M, Zihad SMNK, Rahman MS, Akter S, Khan IN, *et al*. A Systematic Review on Anti-diabetic and Cardioprotective Potential of Gallic Acid: A Widespread Dietary Phytoconstituent. Food Rev Int. 2022;38(4):420-39. doi: 10.1080/87559129.2020.1734609.
49. Hannan JM, Ali L, Khaleque J, Akhter M, Flatt PR, Abdel-Wahab YH. Antihyperglycaemic activity of *Asparagus racemosus* roots is partly mediated by inhibition of carbohydrate digestion and absorption, and enhancement of cellular insulin action. Br J Nutr. 2012;107(9):1316-23. doi: 10.1017/S0007114511004284,

PMID 21899804.

50. Kasabri V. *In vitro* Modulation of Pancreatic insulin Secretion and Extra Pancreatic insulin Action, Enzymatic starch digestion and Protein glycation by *Terminalia chebula* Extracts. Eur J Med Plants. 2014;4(7):771-82. doi: 10.9734/EJMP/2014/8496.
51. Sotoudeh R, Hadjzadeh MA, Gholamnezhad Z, Aghaei A. The antidiabetic and antioxidant effects of a combination of Commiphora mukul, Commiphora myrrha and *Terminalia chebula* in diabetic rats. Avicenna J Phytomed. 2019;9(5):454-64. PMID 31516859.
52. Bansode FW, Arya KR, Singh RK, Narender T. Dose-dependent effects of *Asparagus adscendens* root (AARR) extract on the anabolic, reproductive, and sexual behavioral activity in rats. Pharm Biol. 2015;53(2):192-200. doi: 10.3109/13880209.2014.913295, PMID 24963947.
53. Mathews JN, Flatt PR, Abdel-Wahab YH. *Asparagus adscendens* (*Shweta musali*) stimulates insulin secretion, insulin action and inhibits starch digestion. Br J Nutr. 2006;95(3):576-81. doi: 10.1079/bjn20051650, PMID 16512944.
54. Kasabri V, Flatt PR, AbdelWahab YH. *In vitro* modulation of pancreatic insulin secretion, extrapancreatic insulin action and peptide glycation by *Curcuma longa* aqueous extracts. J Exp Integr Med. 2014;4(3):187. doi: 10.5455/jeim.170414.or.101.
55. Adhikari R, Jyothi Y, Bora D, Vamsee Veena A. Combined effect of aqueous extract of *Curcuma longa* (linn.) With metformin in diabetes induced neuropathic pain in rats. Asian J Pharm Clin Res. 2015;8:173-7.
56. Thomson H, Ojo O, Flatt P, Abdel Wahab Y. Antidiabetic actions of aqueous bark extract of *Swertia chirayita* on insulin secretion, cellular glucose uptake and protein glycation. J Exp Integr Med. 2014;4(4):268-72. doi: 10.5455/jeim.160814.or.110.
57. Hamza N, Berke B, Cheze C, Marais S, Lorrain S, Abdouelfath A *et al*. Effect of *Centaurium erythraea Rafn*, *Artemisia herba-alba* Asso and *Trigonella foenum-Graecum* L. on liver fat accumulation in C57BL/6J mice with high-fat diet-induced type 2 diabetes. J Ethnopharmacol. 2015 Aug 2;171:4-11. doi: 10.1016/j.jep.2015.05.027, PMID 26023031.
58. Hannan JM, Ali L, Rokeya B, Khaleque J, Akhter M, Flatt PR *et al*. Soluble dietary fibre fraction of *Trigonella foenum-Graecum* (fenugreek) seed improves glucose homeostasis in animal models of type 1 and type 2 diabetes by delaying carbohydrate digestion and absorption, and enhancing insulin action. Br J Nutr. 2007;97(3):514-21. doi: 10.1017/S0007114507657869, PMID 17313713.
59. Nagalievska M, Hachkova H, Sybirna N. *Galega officinalis* L. and Immunological Status in Diabetes Mellitus. InMetformin 2019 Nov 27. IntechOpen.
60. Tv V, R A, G S, George S. Post-translationally modified frog skin-derived antimicrobial peptides are effective against Aeromonas sobria. Microb Pathog. 2017;104:287-8. doi: 10.1016/j.micpath.2017.01.052, PMID 28153544.
61. Wu Y, Qiao R, Chen T, Wu J, Du S. Identification and molecular cloning of novel antimicrobial peptides from skin secretions of the Chinese bamboo leaf odorous frog (*Odorrana versabilis*) and the North American pickerel frog (*Rana palustris*). J Trad Chin Med Sci. 2017;4(3):297-305. doi: 10.1016/j.jtcms.2017.07.007.
62. Grassi L, Maisetta G, Maccari G, Esin S, Batoni G. Analogs of the frog-skin antimicrobial peptide temporin 1Tb exhibit a wider spectrum of activity and a stronger antibiofilm potential as compared to the parental peptide. Front Chem. 2017;5:24. doi: 10.3389/fchem.2017.00024, PMID 28443279.
63. Chen C, Mangoni ML, Di YP. *In vivo* therapeutic efficacy of frog skin-derived peptides against *Pseudomonas aeruginosa*-induced pulmonary infection. Sci Rep. 2017;7(1):8548. doi: 10.1038/s41598-017-08361-8, PMID 28819175.
64. Bartels EJH, Dekker D, Amiche M. Dermaseptins, Multifunctional antimicrobial peptides: A review of their pharmacology, effectivity, mechanism of action, and possible future directions. Front Pharmacol. 2019;10:142. doi: 10.3389/fphar.2019.01421, PMID 31849670.
65. Pantic JM, Jovanovic IP, Radosavljevic GD, Gajovic NM, Arsenijevic NN, Conlon JM *et al*. The frog skin host-defense peptide frenatin 2.1 S enhances recruitment, activation and tumoricidal capacity of NK cells. Peptides. 2017;93:44-50. doi: 10.1016/j.peptides.2017.05.006, PMID 28526557.
66. Vineeth Kumar TPVK, Asha R, Shyla G, George S. Identification and characterization of novel host defense peptides from the skin secretion of the fungoid frog, Hydrophylax bahuvistara (Anura: Ranidae). Chem Biol Drug Des. 2018;92(2):1409-18. doi: 10.1111/cbdd.12937, PMID 28072492.
67. Shi D, Hou X, Wang L, Gao Y, Wu D, Xi X *et al*. Two novel dermaseptin-like antimicrobial peptides with anticancer activities from the skin secretion of *Pachymedusa dacnicolor*. Toxins. 2016;8(5):144. doi: 10.3390/toxins8050144, PMID 27187467.
68. Crowe Jr JE. Treating flu with skin of frog. Immunity. 2017;46(4):517-8. doi: 10.1016/j.immuni.2017.04.007, PMID 28423328.
69. Holthausen DJ, Lee SH, Kumar VT, Bouvier NM, Krammer F, Ellebedy AH *et al*. An amphibian host defense peptide is virucidal for human H1 hemagglutinin-bearing influenza viruses. Immunity. 2017;46(4):587-95. doi: 10.1016/j.immuni.2017.03.018, PMID 28423338.
70. Shartouny JR, Jacob J. Mining the tree of life: Host defense peptides as antiviral therapeutics. InSeminars in Cell and Developmental Biology 2019;88. Academic Press.
71. Lima SMF, Freire MS, Gomes ALO, Cantuária APC, Dutra FRP, Magalhães BS *et al*. Antimicrobial and immunomodulatory activity of host defense peptides, clavanins and LL-37, *in vitro*: An endodontic perspective. Peptides. 2017;95:16-24. doi: 10.1016/j.peptides.2017.07.005, PMID 28712894.
72. Lacombe C, Piesse C, Sagan S, Combadière C, Rosenstein Y, Auvynet C. Pachymodulin, a new functional formyl peptide receptor 2 peptidic ligand isolated from frog skin has Janus-like immunomodulatory capacities. J Med Chem. 2015;58(3):1089-99. doi: 10.1021/jm501018q, PMID 25587631.
73. Darrel F. Amphibian species of the world: An online reference. Version 6; 2017. Available from: http://research.amnh.org/herpetology/amphibia/index.html. New York: American Museum of Natural History. [accessed Mar 10, 2020].
74. Liedtke HC. AmphiNom: An amphibian systematics tool. Syst Biodivers. 2019;17(1):1-6. doi: 10.1080/14772000.2018.1518935.
75. Frost D. New York: American Museum of Natural History; 2019. Amphibian species of the world: An online reference. Version 6.0 [internet] [cited 9/13/2022].
76. Evans BJ. Genome evolution and speciation genetics of clawed frogs (Xenopus and Silurana). Front Biosci. 2008;13:4687-706. doi: 10.2741/3033, PMID 18508539.
77. Conlon JM, Mechkarska M, Abdel-Wahab YH, Flatt PR. Peptides from frog skin with potential for development into agents for Type 2 diabetes therapy. Peptides. 2018;100:275-81. doi: 10.1016/j.peptides.2017.09.001, PMID 28887047.
78. Matthijs S, Ye L, Stijlemans B, Cornelis P, Bossuyt F, Roelants K. Low structural variation in the host-defense peptide repertoire of the dwarf clawed frog *Hymenochirus boettgeri* (Pipidae). PLOS ONE. 2014;9(1):e86339. doi: 10.1371/journal.pone.0086339, PMID 24466037.
79. Mechkarska M, Prajeep M, Coquet L, Leprince J, Jouenne T, Vaudry H *et al*. The hymenochirins: A family of host-defense peptides from the Congo dwarf clawed frog *Hymenochirus boettgeri* (Pipidae). Peptides. 2012;35(2):269-75. doi: 10.1016/j.peptides.2012.03.029, PMID 22497805.
80. Mechkarska M, Prajeep M, Radosavljevic GD, Jovanovic IP, Al Baloushi A, Sonnevend A *et al*. An analog of the host-defense peptide hymenochirin-1B with potent broad-spectrum activity against multidrug-resistant bacteria and immunomodulatory properties. Peptides. 2013;50:153-9. doi: 10.1016/j.peptides.2013.10.015, PMID 24172540.
81. Li Y, Zhang Y, Wu M, Chang Q, Hu H, Zhao X. Improving selectivity, proteolytic stability, and antitumor activity of Hymenochirin-1B: A novel glycosylated staple strategy. ACS Chem Biol. 2019;14(3):516-25. doi: 10.1021/acschembio.9b00046, PMID 30789695.
82. Conlon JM, Prajeep M, Mechkarska M, Coquet L, Leprince J, Jouenne T *et al*. Characterization of the host-defense peptides from skin secretions of Merlin's clawed frog *Pseudhymenochirus merlini*: Insights into phylogenetic relationships among the Pipidae. Comp Biochem Physiol Part D Genomics Proteomics. 2013;8(4):352-7. doi: 10.1016/j.cbd.2013.10.002, PMID 24212286.
83. Dubey V, Owusu-Apenten R, Tripathi S, Singh UP, Semwal A. Prospected epigenetic moderators from natural sources and drug of class NSAIDS as effective treatment options to Prostate cancer. J Acute Dis. 2017;6(4):145-53. doi: 10.12980/jad.6.20170401.
84. Dubey V, Owusu-Apenten RK. Enhanced growth-inhibitory effect of microemulsified curcumin formulation in human prostate cancer LNCaP Cells. Br J Pharm Res. 2015;5(3):209-16. doi: 10.9734/BJPR/2015/14475.
85. Owusu-Apenten RK, Dubey V. Curcumin restores glutathione-S-transferase activity for LNCaP prostate cancer cells. Pure Appl Chem Sci. 2014;2(2):61-72.
86. Mostafa AA, Al-Askar AA, Almaary KS, Dawoud TM, Sholkamy EN, Bakri MM. Antimicrobial activity of some plant extracts against bacterial strains causing food poisoning diseases. Saudi J Biol Sci. 2018;25(2):361-6. doi: 10.1016/j.sjbs.2017.02.004, PMID 29472791.
87. Egamberdieva D, Wirth S, Behrendt U, Ahmad P, Berg G. Antimicrobial activity

of medicinal plants correlates with the proportion of antagonistic endophytes. Front Microbiol. 2017;8:199. doi: 10.3389/fmicb.2017.00199, PMID 28232827.

88. Arbab AH, Parvez MK, Al-Dosari MS, Al-Rehaily AJ. *In vitro* evaluation of novel antiviral activities of 60 medicinal plants extracts against hepatitis B virus. Exp Ther Med. 2017 Jul 1;14(1):626-34. doi: 10.3892/etm.2017.4530, PMID 28672977.
89. Seo DJ, Lee M, Jeon SB, Park H, Jeong S, Lee BH *et al*. Antiviral activity of herbal extracts against the hepatitis A virus. Food Control. 2017 Feb 1;72:9-13. doi: 10.1016/j.foodcont.2016.07.028.
90. De Souza JC, Piccinelli AC, Aquino DF, de Souza VV, Schmitz WO, Traesel GK *et al*. Toxicological analysis and antihyperalgesic, antidepressant, and anti-inflammatory effects of *Campomanesia adamantium* fruit barks. Nutr Neurosci. 2017;20(1):23-31. doi: 10.1179/1476830514Y.0000000145, PMID 25116451.
91. Younus I, Siddiq AA. Behavioral evidence of antidepressant-like activity of Raphanus sativus L. var. caudatus in mice. Afr J Tradit Complement Altern Med. 2017;14(3):142-6. doi: 10.21010/ajtcam.v14i3.15, PMID 28480425.
92. Nile SH, Nile AS, Keum YS. Total phenolics, antioxidant, antitumor, and enzyme inhibitory activity of Indian medicinal and aromatic plants extracted with different extraction methods. 3 Biotech. 2017;7(1):76. doi: 10.1007/s13205-017-0706-9, PMID 28452024.
93. Tchuenguem RT, Kechia FA, Kuiate JR, Dzoyem JP. Ethnopharmacological survey, antioxidant and antifungal activity of medicinal plants traditionally used in Baham locality (Cameroon) to treat fungal infections. Arch Med Biomed Res. 2017;3(2):91-103. doi: 10.4314/ambr.v3i2.5.
94. Rodrigues CF, Gaeta HH, Belchor MN, Ferreira MJ, Pinho MV, Toyama Dde O *et al*. Evaluation of Potential Thrombin Inhibitors from the White Mangrove (*Laguncularia racemosa* (L.) C.F. Gaertn.). Mar Drugs. 2015 Jul;13(7):4505-19. doi: 10.3390/md13074505, PMID 26197325.
95. Reid G. Microbes in food to treat and prevent disease. Expert Rev Precis Med Drug Dev. 2018;3(2):79-81. doi: 10.1080/23808993.2018.1429217.
96. Silva MR, Almeida AC, Arruda FV, Gusmao N. Endophytic fungi from Brazilian mangrove plant *Laguncularia racemosa* (L.) Gaertn. (Combretaceae): Their antimicrobial potential. Sci Microb Pathog Commun Curr Res Technol Adv. 2011;2:1260-6.
97. Glasenapp Y, Lucas C, Wöltje T, Fohrer J, Papenbrock J. Anti□adhesion activity of tannins isolated from the mangrove *Laguncularia racemosa*. Chem Biodivers. 2019 May;16(5):e1800632. doi: 10.1002/cbdv.201800632, PMID 30835942.
98. Yadav VK, Mishra A. *In vitro* and *in silico* study of hypoglycemic potential of Pterocarpus marsupium heartwood extract. Nat Prod Res. 2019;33(22):3298-302. doi: 10.1080/14786419.2018.1471078, PMID 29726721.
99. Vangalapati B, Manjrekar PA, Hegde A, Kumar A. Pterocarpus marsupium heartwood extract restores learning, memory and cognitive flexibility in a STZ-NA induced diabetes animal model. Int J Pharm Pharm Sci. 2016;8(3):339-43.
100. Perera HK. Antidiabetic effects of *Pterocarpus marsupium* (Gammalu). Eur J Med Plants. 2016 Jan 1;13(4):1-14. doi: 10.9734/EJMP/2016/23930.
101. Kirana H, Srinivasan BP. *Trichosanthes cucumerina* Linn. improves glucose tolerance and tissue glycogen in non insulin dependent diabetes mellitus induced rats. Indian J Pharmacol. 2008;40(3):103-6. doi: 10.4103/0253-7613.42301, PMID 20040935.
102. Vats V, Yadav SP, Biswas NR, Grover JK. Anti-cataract activity of Pterocarpus marsupium bark and *Trigonella foenum-Graecum* seeds extract in alloxan diabetic rats. J Ethnopharmacol. 2004 Aug 1;93(2-3):289-94. doi: 10.1016/j.jep.2004.03.032, PMID 15234767.
103. Singh P, Bajpai V, Gupta A, Gaikwad AN, Maurya R, Kumar B. Identification and quantification of secondary metabolites of *Pterocarpus marsupium* by LC–MS techniques and its *in-vitro* lipid lowering activity. Ind Crops Prod. 2019;127:26-35. doi: 10.1016/j.indcrop.2018.10.047.
104. Nawaz S, Shareef M, Shahid H, Mushtaq M, Sarfraz M. A review of antihyperlipidemic effect of synthetic phenolic compounds. Matrix Sci Medica. 2017;1(1):22-6. doi: 10.26480/msm.01.2017.22.26.
105. Gupta R, Gupta RS. Effect of Pterocarpus marsupium in streptozotocin-induced hyperglycemic state in rats: Comparison with glibenclamide. Diabetol Croat. 2009;38(2):39-45.
106. Kameswara Rao BK, Giri R, Kesavulu MM, Apparao CH. Effect of oral administration of bark extracts of *Pterocarpus santalinus* L. on blood glucose level in experimental animals. J Ethnopharmacol. 2001 Jan 1;74(1):69-74. doi: 10.1016/s0378-8741(00)00344-5, PMID 11137350.
107. Krishna V, Manjunatha B, Vidya S, Jagadeesh Singh S, Manohara Y, Raheman A *et al*. Evaluation of hepatoprotective activity of stem bark of *Pterocarpus marsupium* Roxb. Indian J Pharmacol. 2005 May 1;37(3):165. doi: 10.4103/0253-7613.16213.
108. Ben Abdallah Kolsi R, Ben Gara A, Chaaben R, El Feki A, Patti FP, El Feki L *et al*. Anti-obesity and lipid lowering effects of *Cymodocea nodosa* sulphated polysaccharide on high cholesterol-fed-rats. Arch Physiol Biochem. 2015 Oct 20;121(5):210-7. doi: 10.3109/13813455.2015.1105266, PMID 26599414.
109. Ben Abdallah Kolsi R, Ben Gara A, Jardak N, Chaaben R, El Feki A, El Feki L *et al*. Inhibitory effects of Cymodocea nodosa sulphated polysaccharide on α-amylase activity, liver-kidney toxicities and lipid profile disorders in diabetic rats. Arch Physiol Biochem. 2015 Oct 20;121(5):218-27. doi: 10.3109/13813455.2015.1107588, PMID 26599334.
110. Ben Abdallah Kolsi R, Ben Salah H, Jardak N, Chaaben R, El Feki A, Rebai T