

The Potential Use of Leech, Dhab Lizard and Mudskippers for Men's Sexual Health: A Scoping Review

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ABSTRACT

Introduction: The use of animals for medical treatment or zootherapy has been reported all over the world. This study aims to assess the potential use of leech, dhab lizard and mudskipper for men's sexual health, particularly in the treatment of erectile dysfunction (ED). **Methods:** Using systematic review study design, relevant articles were located from three electronic databases, which are OvidMEDLINE, Google Scholar and PubMed. A total of 180 articles were searched from the electronic databases and 10 journal articles were included in the study. Another 12 articles were identified from hand-search of reference list. **Results:** There were limited human studies reporting the use of the leech, mudskipper and dhab lizard for men's sexual health. Hence, the efficacy and safety of the aforementioned zootherapy were not able to be determined. **Conclusion:** A recommendation for well-designed studies in vitro and in vivo are needed before the animal's product and derivatives can be used in clinical trials.

KEYWORDS: Leech, Dhab Lizard, Mudskipper, Men's Sexual Health, Erectile Dysfunction

INTRODUCTION

Men's sexual health is frequently related to men's sexual dysfunction, which prevents a man from gaining sexual satisfaction due to medical and psychological conditions such as erectile dysfunction (ED), premature ejaculation (PE), and hypogonadism [1]. Since ED is a widespread issue affecting men worldwide, it frequently receives special attention. In 2011, estimates of the prevalence of ED in Malaysia ranged from 22.4 to 59%, and the incidence was reported to increase with age [2]. Meanwhile, it was stated that more than 20 million men in the United States had ED in 1999, with the estimation that 322 million men worldwide will have the condition by 2025 [3]. ED is defined as the inability to achieve or maintain an erection sufficient for satisfactory sexual performance [4]. It is frequently associated with chronic diseases such as diabetes,

kidney disease, atherosclerosis and vascular disease affecting the arteries, smooth muscle and fibrous tissue resulting in altered blood flow to and from the penis causing ED [3]. Hormonal, vascular, drug-induced and ageing are also some of the common causes of ED [5, 6].

The management for ED varies from localised treatments, such as intracavernosal, intraurethral or topical, to systemic treatment. Currently, the standard therapeutic treatment for ED includes the use of oral phosphodiesterase type 5 inhibitors (PDE-5 inhibitors) such as sildenafil, tadalafil, vardenafil and avanafil [2, 3, 6, 7]. PDE-5 inhibitor has become the first-line therapy for ED since 1988 as it is convenient, practical, rapid onset of action, and tolerable [8]. Apart from medical treatment, other alternative therapies for ED include ginseng, yohimbine (an African bark tree), ginkgo biloba, *lepidium meyenii* (the Maca plant).



These conventional plants and herbs are claimed to provide aphrodisiac properties for those with sexual health issues [6, 9-13]. Another treatment strategy for the problem is zootherapy, based on medication derived from animals or their by-products [9]. Since the bioactive principle of this alternative medication is frequently unclear, additional information on the potential mechanism in treating disease is required.

There are several alleged claims on the medical use of animal-based products, namely leech, dhab lizard, and mudskipper, for men's sexual health treatment. For instance, fortifying oils made from the aforementioned animals are widely advertised as being used to improve sexual performance, and some are sold at exorbitant amounts on internet marketplaces. These kinds of animal-based products are in demand since they are thought to be associated with magic healing or traditional medicine, which may improve men's sexual health, especially ED [14]. The traditional method, such as zootherapy or phytotherapy, in treating the condition is favoured for numerous reasons, including its ecological, cultural, and economic aspects [15]. In addition, some individuals rely on zootherapy since access to modern medical facilities is limited due to several factors including lack of awareness, expensive medications, and inadequate transportation [16]. However, the use of phytotherapy and zootherapy in men's sexual health treatment is not recommended as both have their downsides and have not yet been substantiated or disproven by scientific evidence [9].

Improper use of traditional products with inadequate supervision and poor regulation of the product's ingredients can adversely impact a person's ability for sexual function [17]. Despite claims by the traditional medicine practitioners that their medication has no negative effects, taking traditional medicine in excess of what is advised might cause a deadly prolonged erection. In addition, overuse of animals or plants in traditional medicine would interfere with the ecology, resource management, and conservation [15].

To date, limited studies have evaluated the available information on the use of animal products and derivatives for men's sexual dysfunction. Reviewing the existing data on the safety and efficacy of leeches, dhab lizards, and mudskippers is important, given the growing demand for these products in the Malaysian

market for men's sexual health. The current study, therefore, aimed to conduct a scoping review to assess the available evidence on the potential use of leech, dhab lizard and mudskipper in men's sexual health treatment reported worldwide. This will aid in identifying and raising knowledge of the proper use of these animal products in men's sexual health.

MATERIALS AND METHODS

This study was conducted as a scoping review of available evidence that reported the potential use of leeches, dhab lizards and mudskippers for men's sexual health. The articles were searched and identified systematically from three electronic databases, Ovid MEDLINE, PubMed and Google Scholar, from inception till March 2022. The keywords and Medical Subject Headings (MeSH) used to locate the relevant article were as follows; "Sexual Health" OR "Men's health" OR "Erectile Dysfunction" AND in combination with "Leech" OR "*Hirudo medicinalis*" OR "Leech Therapy" OR "Dhab" OR "*Uromastyx*" OR "Spiny-tailed lizard" OR "Mudskipper" OR "*Oxudercinae*". Boolean operators such as "AND" and "OR" were used to increase the sensitivity and specificity of the search where appropriate. The retrieved paper's citation was used to find further relevant papers. All retrieved articles were transferred to a reference manager, Mendeley.

All references identified from the search strategy were screened and assessed using inclusion and exclusion criteria. The inclusion criteria included articles that reported the use of leeches, dhab lizards and mudskippers or their derivatives for men's sexual health. The articles included in the review include studies *in vivo*, *in vitro*, clinical studies, case reports, short communications, survey or review articles. In addition, grey literature such as magazines, newspapers and conference proceeding papers, which reported the claims or use of these three animal-based therapies for sexual health treatment were also included in this study. Articles published in languages other than English and full articles that were inaccessible were excluded from this study.

The initial screening was done through the title, followed by the abstract and full article by NIS and checked by MFR. The objective of screening and

executing the articles was to determine and select the most relevant published paper to be used and included in the review. The exclusion process using titles or abstract articles by NIS only occurred if the reason for exclusion was clear. If there was uncertainty or ambiguity, the article was not excluded, and each research team (NIS, MFR, EH) then reviewed the articles. Then, NIS, MFR and EH assessed all excluded 'full text' articles independently to ensure the validity of the process and that any disagreements on whether a study should be included/excluded were resolved through consensus.

Important study characteristics such as author, country, year, type of article, study design, study objective, the claims on men's sexual health, other reported findings and side effects of leech, dhab lizard and mudskippers on men's health were extracted from all relevant articles and recorded in the extraction table. Two research team members, MFR and NIS, extracted the data individually and compared the results for similarities and discrepancies. Any disagreements were discussed with other team members, EH, NSS, and AHI and a consensus was reached based on majority agreement.

Data analysis was conducted through narrative synthesis of the articles by evaluating and comparing the studies done in the area. The results were critically assessed and summarised according to the authors, year of publication and reference type, country, study type, field of the study, study objective, delivery method, methodology, key findings on sexual health, other reported findings and reported adverse/side effects.

RESULTS

A total of 180 articles were located in three electronic databases: five from Ovid MEDLINE, 21 from PubMed and 154 from Google Scholar databases. Following screening, only ten articles fulfilled the inclusion and exclusion criteria and were included in the study. Articles were removed from the study (n=158) due to duplication (n = 5), non-English articles (n = 1), not fully accessible (n = 6), titles not related to interest (n =115), pure zoologist topic (n = 5) and the outcome was not related to sexual health (n = 26). A total of 12 articles were located using a hand search of reference

lists. Of the 22 articles included, 19 were research articles, and three were grey works of literature: newspaper, magazine and conference proceeding papers. The Prism flow chart that summarises the screening process for article selection is presented in Figure 1.

Leech

There were nine papers that reported the use of leech treatment for enhancing sexual function. This includes using leech as oil or injections with leech-centipede granules (LCG). The included articles consisted of two case reports [18, 19], one proceeding paper [20], five journal articles reporting studies *in vivo* [21-25], and a review article on the therapeutic use of leech [26]. The studies *in vivo* were mainly conducted in China (n = 4) and Iran (n = 1), while case reports on human use of leeches were from Iran (n = 1) and Indonesia (n = 1). Only one proceeding paper from Russia reported a clinical trial finding and one review article by researchers from India.

Four research studies reportedly employed LCG as an injection. In their studies, rats with diabetes mellitus-induced erectile dysfunction (DIED) were injected with LCG, and the result exhibited improvement in erection frequency (n = 2) and ED (n = 2) [21-24]. Bioactive substances such as ICP/MAP, SOD, NO, cGMP and cAMP levels, PDE5, PKC and CaSR/PLC/PKC signalling pathways were reported to be potential modes of action of LCG on erectile function. In their studies, Wang et al. (2021) and Ma et al. (2020) reported that LCG, through inhibition of several expressions in the PKC pathway, may protect penile endothelial function and hence improve erectile function.

Suction methods with leeches were reported in three articles. In one study, leech was reported to be applied directly into the male genitalia area; one was a study *in vivo* on rats [25], and two were case reports on humans [19, 20]. In a study by Asgari et al. (2017), leeches were directly applied twice at one-hour intervals on the penile shaft of a man who experienced priapism. The patient was discharged after three days, and the priapism was reported to resolve within a month [19]. In the rat study, leeches were used on the rat's testicular torsion [25]. The study revealed that the effect of leech

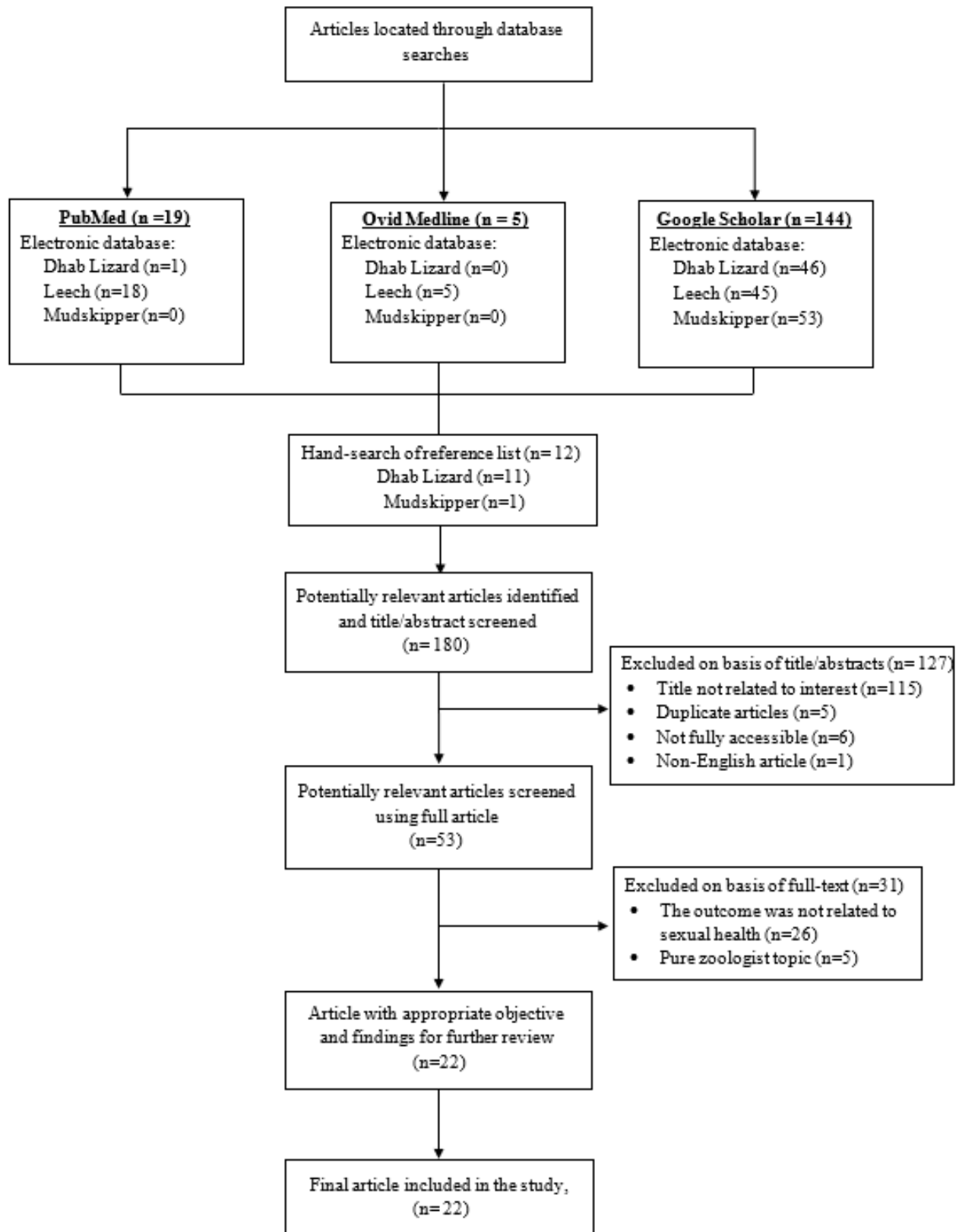


Figure 1 PRISMA flow chart on the summary of the screening process

therapy increased the progressive motility and reduced oxidative damage, improving sperm quality and decreasing histopathological damage as well as reducing testicular apoptosis. A clinical trial study reported as a proceeding paper by Sukhov, K. (2016), investigated the effect of leech suction on 34 men aged 27 to 64 years with ED and with various comorbid conditions. The author discovered that, although the healing process was long, which was one to eight months, there was an improvement in the patients' sexual health following leech therapy.

Only one article reported a case of adverse effects of using leech oil for genital augmentation. The case report by Paramita et al. (2016) from Indonesia documented the development of penile ulcers and swelling on the shaft penis following leech oil injection. So far, this is the only article that reported the use of leech oil treatment for men's sexual function. The summary of articles discovered related to leeches used for sexual health is presented in Table 1.

Dhab Lizard

In the current study, 11 articles on dhab lizards or their derivatives for sexual health were included. Ten articles were journal articles [16, 27-35], and one was a newspaper article [36]. There were six articles from Pakistan, one article and one newspaper report from Malaysia and one article each from India, European Union (EU), and Suriname. The identified articles consisted of three mixed-method study designs: one with an ethnozoological survey, one with a cohort study, and four were review articles. None were conducted as *in vitro*, *in vivo* or clinical studies. Two articles reported reviews on dhab lizard's taxonomy and biodiversity [31, 35], two on commerce and trading-related activity [30, 33], and seven included claims on its traditional medicine use [16, 27-29, 32, 34, 36]. The mixed method studies by Altaf et al. (2018) and Altaf et al. (2020) revealed that there was a high-fidelity level (FL), referring to high use by the local people of dhab lizards or *uromastix spp.* for sexual impotence by people in River Chenab, Punjab (n = 24; 100%), Jhelum (n = 72; 72%) and Lahore (n = 72; 72.73%).

The high FL of the dhab lizard indicates a recommendation for further bioactive composition analysis of the animal product. Furthermore, several review articles reported the use of dhab lizard derivative using the animal's fat for enhancement in sexual performance, male sexual organ debility remedy and ED treatment [16, 29, 32, 35, 34]. Additionally, two articles from Malaysia and the EU and one newspaper report from Malaysia reported on the availability and trading activities of dhab lizard's products in the market and the potential extinction of the animal due to it being hunted for its medicinal value [30, 33, 36]. In the articles, the dhab lizard, known as the spiny-tailed lizard, was claimed to possess medicinal value and was used as part of traditional medicinal oil preparation in Malaysia [31, 33]. The report in Utusan Melayu, 2014 reported that the spiny-tailed lizard-based product for sexual dysfunction has been promoted to treat diseases in Malaysia since 1995 [30]. Two taxonomy and biodiversity review papers from Suriname and India addressed ecological data and the therapeutic potential of the dhab lizard, particularly in sexual impotence remedy, which possesses great medicinal value [31, 35]. The articles reported on the dhab lizard's use for sexual health are summarised in Table 2.

Mudskipper

In the current study, only two articles were included on the usage of mudskipper for sexual health. A cross-sectional survey by Hayatul SS et al. (2020) on local communities' perceptions of the use of mudskipper fish for traditional medicinal purposes in Terengganu, Kelantan, and Pahang, three states of East Coast Peninsular Malaysia. The authors discovered that most respondents believe the fish could be utilised to treat ED based on their own experiences consuming the fish as well as the experiences of family members who had similar illness [37]. Additionally, a magazine article by Khaironizam and Norma Rashid (2000) from Science University and University of Malaya, Malaysia, respectively, includes claims by the locals at Kuala Selangor and Morib's on mudskipper's therapeutic properties in treating men's sexual health [38]. The summary of articles reported on the potential use of mudskippers for sexual health is presented in Table 3.

Table 1 Summary of the included study on potential use of leech on sexual health (n = 9)

No	Authors, Year of Publication, Type of Article (Journal article, grey literature)	Country	Study Design (<i>in vivo</i> , <i>in vitro</i> , clinical)	Field of Study	Study Objective	Claims on Sexual Health	Other reported findings	Reported adverse/ side effect
1	Ma JX, Wang B, Li HS, Yu J, Hu HM, Ding CF, et al., 2021 Journal Article	China	<i>In vivo</i> (Animal)	Ethnopharmacology	To identify bioactive components and LCG in DMED rat	1. LCG increased the testosterone, erection frequency, ICP/MAP, SOD, NO, cGMP and cAMP levels and decreased AGEs level 2. LCG treatment might enhance erectile functioning in DMED rats	LCG could possibly treat DMED via regulation of calcium channels and insulin signal transduction	Oxidative stress and inflammation occurred
2	Wang JS, Li X, Chen ZL, Feng JL, Bao BH, Deng S, et al., 2021a, Journal Article	China	<i>In vivo</i> (Animal)	Ethnopharmacology	To study the mechanism of leech-centipede medicine related to the PKC signalling pathway in treating erectile dysfunction in DMED rats	Leech-Centipede therapy can treat erectile dysfunction by inhibiting the expression of PKC signalling pathway in DMED rats.	1. Leech-Centipede medicine can reduce oxidative stress injury and improve antioxidant capacity 2. Leech-Centipede had protective effect on endothelial function, anti-platelet activation	-

3	Abdualkader AM, Ghawi AM, Alaama M, Awang M, Merzouk A., 2013, Journal Article	India	Review	Ethnopharmacology	To review the therapeutic application of leech in various field	Leeching-treated patients observed normal function for erection	Leeching help to relieve post-operative venous congestion for penile replantation and gives normal functions	-
4	Asgari SA, Rostami S, Teimoori M., 2017, Journal Article	Iran	Case Report (Human)	Public Health	To treat patient with priapism using leech therapy	1. The patient reported significant decreased of pain and perineal swelling after 2 days and completely resolved over one month 2. Leech therapy can be used in treating priapism	Hirudotherapy act as anti-inflammatory and pain treatment	Bacterial infection and sepsis
5	Davoodi F, Taheri S, Raisi A, Rajabzadeh A, Zakian A, Hablolvarid MH, et al., 2021, Journal Article	Iran	<i>In vivo</i> (Animal)	Ethnopharmacology	To evaluate the mechanism of leech therapy in protecting testicular tissue from ischemia/reperfusion damage in rats	Leech therapy significantly increased the progressive motility and reduced the non-progressive motility of sperm cells	Sperm morphology and coiled tail was increase with reduce damage to testicular tissue due to antioxidant, anti-inflammatory and anti-apoptotic effects	-
6	Sukhov K., 2016, Proceeding paper	Russia	Clinical Trial (Human, n = 34)	Hirudotherapy	To assess potential use of hirudotherapy in treating erectile dysfunction among men with various comorbid conditions	Most patients reported complete recovery of sexual function and the recovery was long and persistent	91.2% of patients reported hirudotherapy help in recovery of sexual function in between 2-8 weeks of therapy.	-
7	Paramita K, Prakoeswa CR., 2016, Journal Article	Indonesia	Case Report (Human)	Public Health	To review the clinical manifestation and management of penile ulcer caused	Lintah oil penile injection caused multiple adverse effect with no improvement	Leech oil used was claimed for genital enlargement	Irritation and painful penile ulcer due to lintah oil injection

					by leech oil injection	on the sexual health and penis size.		
8	Wang JS, Feng JL, Li X, Chen ZL, Bao BH, Deng S, et al., 2021b, Journal Article	China	<i>In Vivo</i> (Animal)	Ethnopharmacology	To assess the effect and mechanism of leech-centipede in treating erectile function in DMED rats	1. There was a significant improvement in erectile function among DMED rats after 8 weeks. 2. Erectile dysfunction can be treated in DMED rats by regulating the expression of cGMP, NOS, PDE5-related molecule in PDE5 pathway using leech-centipede medicine	LCG improve blood glucose level, testosterone secretion level, repairing pathological and ultrastructural damage of the penis cavernous body	This drug potentially can cause headache, backache or flushing during application
9	Ma JX, Wang B, Ding CF, Li HS, Jiang XJ, Wang CY, et al., 2020, Journal Article	China	<i>In Vivo</i> (Animal)	Ethnopharmacology	To assess the efficacy of LCG through CaSR/PLC/PKC signalling	LCG treatment significantly improved erectile function of DMED rats by inhibiting CaSR/PLC/PKC signalling pathway.	1. LCG improve vascular endothelial injury, the ability of vasodilation and decrease the penile fibrosis 2. LCG decrease cell apoptosis and enhance nitric oxide level to ameliorate erectile function	-

LCG = Leech-centipede granules; DMED = Diabetes mellitus-induced erectile dysfunction; ICP/MAP = Intracavernous pressure / Mean arterial pressure; SOD = Superoxide dismutase; NO = Nitric oxide; cGMP = Cyclic guanosine monophosphate; cAMP = Cyclic adenosine monophosphate; AGEs = Advanced glycation end products; PKC = Protein kinase C; PDE5 = phosphodiesterase; NOS = NO synthase; CaSR = Calcium-sensing receptor; PLC = Phospholipase C; ED = Erectile dysfunction

Table 2 Summary of the included study on the potential use of dhab lizard on sexual health (n = 11)

No	Authors, Year of Publication, Type of Article (Journal article, grey literature)	Country	Study Design (<i>in vivo</i> , <i>in vitro</i> , clinical)	Field of Study	Study Objective	Claims on Sexual Health	Other reported findings	Reported adverse/ side effect
1.	Altaf M, Abbasi AM, Umair M, Amjad MS, Irshad K, Khan AM., 2020, Journal Article	Pakistan	Observational Study (Mixed Method)	Ethnobiology and Ethnomedicine	To record the traditional uses of herptile and fish species among the native around the River Chenab, Punjab Pakistan.	In treating sexual impotence, the study found that <i>Uromastyx spp.</i> (Dhab lizard) had 100% fidelity level (FL).	Fats and oils were utilised for erectile dysfunction treatment.	-
2.	Arshad M, Ahmad M, Ahmed E, Saboor A, Abbas A, Sadiq S., 2014, Journal Article	Pakistan	Observational Study (Mixed Method)	Ethnobiology and Ethnomedicine	To compile and analyse native cultures' knowledge of plants and animals, with a focus on ethnobotanical and ethnozoological components.	The study found that the locals utilise an extract of the <i>Uromastyx Hardwickii</i> (Saanda) for massaging their bodies and to increase their sexual potency.	-	-
3.	Altaf M, Umair M, Abbasi AR, Muhammad N, Abbasi AM., 2018, Journal Article	Pakistan	Observational Study (Ethnozoological Field Survey)	Ethnobiology and Ethnomedicine	To report animal-based traditional therapies used by the native from Jhelum and Lahore districts of the Punjab province, Pakistan.	1. Saara Hardwickii (Spiny-tailed ground lizard) reveals noticeably high Relative Importance (RI) which is 1.56 and 1.21 in sexual enhancement for Jhelum and Lahore district respectively. 2. Additionally, the study	-	-

4.	Ehsan M, Khalil MZ, Rasool F., 2018, Journal Article	Pakistan	Review	Medical	To examine any non-surgical techniques that could lengthen or thicken a natural penis.	reveals high FL for Saara Hardwick for sexual enhancement that is 72.00 and 72.73 for Jhelum and Lahore respectively.	A number of people can be seen claiming to have enlarged penis due to a purported so-called medicine named Sandy Ka Tail (Saara Hardwickii Oil), which is extracted from the Saara Hardwickii spiny-tailed lizard.	There is no assurance and demonstrated study that has proven Saanda Oil can broaden the span of a penis and grow the extent of a penis.	-
5.	Ahmad S, Akram M, Riaz M, Munir N, Mahmood Tahir I, Anwar H, et al., 2021, Journal Article	Pakistan	Review	Zootherapy	To investigate the zoo therapeutic elements of Cholistan desert used for the survival and treatment of the native inhabitants with limited resources.	1. The treatment of male sexual organ debility reportedly used the spiny-tailed lizard known as <i>Sandha or Saanda</i> , according to 41 informants in the study. 2. According to 19 informants, the Geyr's spiny-tailed lizard was utilised to treat female breast weakness and male sexual organ debility. both paralysis and arthritis	1. The fat was obtained by the incision to the animal 2. Mode of administration: External	-	
6.	RA Mans D, Pawirodihardjo J, Djotaroeno M, Friperon P., 2021,	Suriname	Review	Biodiversity	To highlight some of the bioactive substances derived from reptiles and	In parts of northern Africa and India, the oil derived from the fat of spiny-tailed lizards of the genus	-	-	

	Journal Article				therapeutic potential of some of them.	<i>Uromastyx</i> has been long been used as an embrocation topical treatment for sexual impotence and as an aphrodisiac.		
7.	Ching OO, Chng SC., 2016, Journal Article	Malaysia	Short Communication	Trade and Commerce	To determine the availability of spiny-tailed lizard-based products used for medicinal usage in Kuala Lumpur and the State of Selangor	Traditional medicine products from Malaysia that purportedly contain spiny-tailed lizard parts and derivatives are being sold both legitimately and illegally for claimed medicinal uses including sexual enhancement.	For more than 20 years, spiny-tailed lizard-based products have been actively promoted and made available for purchase, indicating a constant supply and demand.	-
8.	Utusan Melayu, 2014, Grey literature	Malaysia	Newspaper	-	-	Since at least 1995, product derived from spiny-tailed lizards have been advertised in Malaysia as a remedy for a variety of ailments, including erectile dysfunction.	The use of spiny-tailed lizard-based products had been promoted to treat diseases like diabetes, heart disease, hypertension, gout, and renal issues.	-
9.	Knapp A., 2004, Journal Article	European Union (EU)	Review	Trading	An assessment of the global trade in Spiny-tailed Lizards, <i>Uromastyx</i> with a focus on the role of the European Union.	Muslim communities in Malaysia utilized a traditional medicinal oil that was made from the spiny-tailed lizard, often known as the Dabb Lizard (<i>Uromastyx spp.</i>).	Spiny-tailed lizards are illegally imported and marketed into Southeast Asia for its alleged medicinal benefits.	-

10.	Mahmood T, Shah SM, Rais M, Nadeem MS., 2011, Journal Article	Pakistan	Observational Study (Mixed Method)	Animal & Plant Sciences	To gather data on the trade of animal species in selected markets; Goodri market, Multan and College Road market, Rawalpindi.	Spiny-tailed lizard (<i>Uromastyx Hardwickii</i>) was one of the renowned reptile species that were marketed in Multan and Rawalpindi Market for its medicinal purpose particularly in pain and sexual disorder treatment.	-	-
11.	Das SK, Dookia S, Das K, Dutta SK., 2013, Journal Article	India	Observational Study (Quadrat sampling method)	Taxonomy	To gather information about the ecology of spiny-tailed lizards species based on research done in Tal Chhapar Wildlife Sanctuary, Sujangarh Tehsil, India.	The spiny-tailed lizard is commercialized and exploited for its meat, skin and oil, the latter of which was thought to have significant medicinal value.	-	-

FL = Fidelity Level; RI = Relative Importance

Table 3 Summary of the included study on potential use of mudskipper on sexual health (n = 2)

No.	Authors, Year of Publication, Type of Article (Journal article, grey literature)	Country	Study Design (in vivo, in vitro, clinical, testimonial)	Field of Study	Study Objective	Claims on Sexual Health	Other reported findings	Reported adverse/ side effect
1	Salleh HS, Mohamed WN, Mat NHN, Yusof Y, Syamimi N., 2020, Journal Article	Malaysia	Observational Study (Mixed Method)	Traditional Medicine	To investigate the consumers' knowledge and perceptions towards the use of marine resources for traditional medicinal purposes.	The respondents' belief and acknowledgement of the Mudskipper use in the treatment of erectile dysfunction was founded based on their own experiences as well as the experiences of their family members who had been healed after taking traditional marine-based medicines.	The respondent learned about traditional medicine related to the mudskipper curative properties from their ancestor, who handed it down through the generations.	-
2.	Khaironizam MZ & Norma-Rashid Y., 2000, Magazine	Malaysia	Review	Zoology	To elaborate the importance of mudskipper fish	1. Locals at Kuala Selangor and Morib claimed the mudskipper could be used to treat men' sexual health, lethargy, hypertension and diabetes. 2. The essence of the mudskipper fish is used in some traditional medicine products for massaging and sexual dysfunction treatment.	The mudskipper fish was valuable for conservation of swamp flora and wildlife, medicinal biochemistry, pharmaceutical use, and commercial value.	-

DISCUSSION

To our knowledge, this is the first scoping review done to investigate the potential use of leeches, dhab lizards and mudskippers for sexual health. Despite the growing demand for these products in the market, especially in Malaysia, limited studies were found to investigate the potential use of these animals or their by-products for sexual health. Up to date, only leech studies were discovered to have some case reports on human and studies *in vivo* on rats, which later described the potential pathways and mechanism of action of the combination of LCG for improving sexual function. Meanwhile, the study on dhab lizard only included a combination of qualitative interviews and survey studies of perceptions of local people on the use of the animal for sexual health. For dhab lizard, the review articles only included local claims of its use for sexual dysfunction.

Our scoping review revealed four important studies *in vivo* using LCG on male sexual function in DIED rats. Currently, the study on LCG has not yet reached clinical study. Live leech suction as therapeutic therapy has been widely introduced in medical practice, not only for sexual health but also in reconstructive and microsurgery [26]. In the current study, three articles reported the use of leech suction or bites on male genitalia either in rats ($n = 1$) or humans ($n = 2$) to improve sexual function. Although in the rat studies, the sexual function appears to be improved, the treatment effectiveness in humans was still limited. Only one proceeding paper by Asgari et al. (2017) reported the use of leech suction to treat priapism in humans. The study conducted on 34 patients reported that the majority of patients (91.2%) documented that hirudotherapy helped recover their sexual function. Nevertheless, the proceeding paper did not describe the study protocol clearly. It also had a weak design of the clinical trial with a small sample size ($n = 34$). The paper also did not discuss the potential bioactive compounds or pathways that explain the sexual improvement effect of leech suction [19].

The only study that reported the adverse effect of leech oil injection was the article by Paramita et al. (2016). In the case report, the injection of leech oil, believed to help in penis enlargement, had caused the development of painful ulcers that deteriorated into

multiple wounds. Although the reported case was discovered to be quite common in Indonesia, only the article by Paramita et al. (2017) reported it. Since a limited research study was done investigating the active ingredient of leech oil that potentially aids penis augmentation or development of ulcers, the safety of leech oil used for sexual function is still questionable.

In the current study, the articles reporting the dhab lizard used for sexual health were mostly from Pakistan. This might be due to the geographical condition of Pakistan that supported the dhab lizard habitat. There were several articles that reported the medicinal values and therapeutic properties of dhab lizard related to sexual health. However, these were only based on purported claims and beliefs of the native communities. Currently, there is no study *in vivo* or *in vitro* on dhab lizard and its relationship with sexual health. Despite the lack of scientific evidence regarding the product, the dhab lizard-based products were marketed in various packaging such as capsules, oils, fats, whole dried skins and coffee mix-sachets with their claimed medicinal value [30]. In addition, despite being advertised as the main active ingredient, a false advertisement was reported in which the dhab lizard-based products were not actually presented in the ingredients [30]. Without proper guidelines and scientific evidence, these products might jeopardise the consumer's safety.

It had been observed that dhab oil was in high demand, particularly in e-commerce platforms, with thousands of products sold. The oil is extracted from the dhab lizard's fat obtained by surgical incision to the animal's body and mainly used as an embrocation in preparations of traditional medicinal oil for sexual impotence and sexual disorder treatment by the natives in Malaysia [33, 39]. In South India, the locals believe that the dhab lizard's fat and flesh might contain sex hormones and testosterone and possess aphrodisiac properties [39,40]. Nevertheless, none of the articles reported the standard procedure for dhab lizards' fat oil extraction besides surgical incision. The extraction process of the desired bioactive components from the raw material must be hygienic and is crucial in preventing undesired effects on the consumers to produce safer and quality products [41]. Dhab lizards are expensive; thus, they are intensively sought for their alleged therapeutic properties. As a result, the

consumption has reportedly endangered the species [30, 33, 42].

Our findings on mudskipper fish indicate a scarcity of research studies providing scientific evidence that justifies its potential therapeutic use in men's sexual health. There was only one survey study, and one magazine article reported on the mudskipper fish used for men's sexual health. The mudskipper fish was claimed by the natives in Kuala Selangor and Morib, Malaysia, to possess a curative effect on men's sexual health problems, particularly ED. In the magazine, the raw flesh of the mudskipper fish was reported to possess aphrodisiac properties by the locals in Malaysia as early as 1903 [43]. In a recent survey by Salleh et al. (2020), most of the respondents in Malaysia acknowledged the use of mudskipper fish in ED treatment as their previous generation informed them about the medicinal properties of the marine resource. Over time, the knowledge of the traditional use of the mudskipper fish was then passed down from generation to generation and further assimilated among the locals [37].

A review study by Kumaraguru et al. (2020) in India reported that the locals used the mudskipper fish for its numerous nutritional benefits [44, 45, 46]. Despite limited evidence that supports the efficacy and safety, 'Minyak Belacak,' which includes mudskipper essence and derivatives, was reported to be among the highest revenue earner for products sold in a company located in Malaysia, indicating a huge demand for its use to treat or enhance sexual performance [47]. However, there has been no proper research and investigation done to scientifically prove the potential use of mudskippers for treatment of men's sexual health. Additionally, the medicinal values and traditional use were only purported claims and believed by the author or the natives [38, 44, 45].

This current study was subject to a few limitations. First, there was a lack of information on the direct relationship between the leech, dhab lizard and mudskipper zootherapy with men's sexual health. In addition, since the studies on the use of zootherapy on humans are limited, this limits our discussion on the potential use of these products in clinical trials. Second, most of the information and statements related to men's sexual health in the included studies were limited to

'claimed', 'purported' and 'rumours' without proper scientific evidence, hence impeding the discussion on the efficacy and potential outcomes. Third, this study only included articles that were published in the English language. Hence, it might be missing relevant papers published in other languages. Finally, the nature of the scoping review, which aims to map the existing literature and include topics that have not yet been extensively reviewed, was subject to ambiguous scoping evidence interpretation with a lack of quality appraisal.

CONCLUSION

Despite the huge market demand for leeches, dhab lizard and mudskipper and their derivatives for aphrodisiac properties, there is limited evidence to scientifically prove these animals' potential use for men's sexual health treatment. Moreover, adverse effects such as ulcers that lead to inflammation and infection of the genital area have been reported. Since many of the articles only reported 'claimed,' 'purported,' and 'rumours' for the potential use of leech, mudskipper and dhab lizard zootherapy for men's sexual health based on folklore, little can be gleaned from these reports. Further efforts are required to provide scientific evidence-based medicine by enhancing the quality of reporting primary studies of these animal products or by-products. More well-designed *in vitro* and *in vivo* studies are needed before the animal's product, and derivatives can be used in clinical trials. Understanding the responsible bioactive compounds and their potential mechanism/s of action is needed to understand its potential.

Conflict of interest

Authors declare none.

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Authors' Contribution

All authors wrote, edited, reviewed and revised the final complete version of the article.

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