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Review Article

SESAMUM RADIATUM LEAVES CAN HELP CHILDBIRTH

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Abstract: This study was carried out to verify the ability of *Sesamum radiatum* leaves to facilitate delivery. From this investigation, it can be concluded that *S. radiatum* was toxic plant. This toxicity as those of many drugs can not limit its use for therapeutic purposes. To facilitate childbirth, African populations used low doses that did not cause systemic toxicity in humans. *S. radiatum* aqueous leaf extract induced hypotension which was similar to those of oxytocin (Syntocinon®) and misoprostol (Cytotec®). As misoprostol and oxytocin, *S. radiatum* aqueous leaf extract caused a vasorelaxation and a stimulating effect on uterine smooth muscle contraction. This uterotonic action (prostaglandin-like activity) showed *S. radiatum* ability to mobilize calcium intra-and extra-cellular, which confirms its utéronic property. To summarize, *S. radiatum* had two fundamental properties that justify the use of oxytocic-like substances to facilitate labor namely a uterotonic effect and hypotensive action. This herbal would have a great biomedical interest in the field of obstetrics and gynecology. *Sesamum radiatum* Schum. & Thonn. (Pedaliaceae) can be used to facilitate childbirth in parturient women.

Key**words:** *Sesamum radiatum*, Childbirth, Parturient women, Uterine contractility, Blood pressure, Acute toxicity

INTRODUCTION

Parturition is defined as expulsion, out of maternal genital tract of the fetus and its annexes [1]. It is determined by various factors. Its trigger process which according to Buxton *et al.* [2], is mysterious and physiology remain to be elucidated in general and more specifically in humans [3-5].

Several parameters are associated with childbirth [6,7]. However, it should be noted that physiological factors are the most important determinants. Indeed, they are essential for all parturient women while sociocultural and economic context of childbirth vary or are simply not considered. Individual factors including maternal age, parity, education and marital status, household factors including family size, household wealth, and community factors including socioeconomic status, community health infrastructure, region, rural/urban residence, available health facilities, and distance to health facilities determine place of delivery and these factors interact in diverse ways in each context to determine place of delivery [7-10]. A significant proportion of mothers in developing countries still deliver at home unattended by skilled health workers [11-14]. In sub-saharan Africa and Arab worlds, childbirth concern mature-aged women exclusively. Men and children are kept out of the delivery room. Women give birth more often without the help of professional. Rather, they are assisted by traditional birth attendants (TBAs) whose practices do not comply with the medical standards prescribed by WHO [15]. These TBAs used medicinal plants including *Sesamum radiatum* Schum. & Thonn. (Pedaliaceae).

In Côte d'Ivoire, this plant is known to all rural populations as well as urban. They commonly used this vegetable species to facilitate delivery [16-19]. Indeed, because of its geographical distribution, this herbal is easily accessible. This plant species grows on the whole territory, on the lands and even around habitations [20]. These people can get them easily. Slightly softened fire and expression, *S. radiatum* leaves give an extract that is given to parturient women to facilitate childbirth. However, its extensive use raises questions. The problem is that the use of these herbals is done without knowledge of the real effects of these. This plant species can really facilitate the deliveries? How this medicinal plant can help childbirth? Or simply, *S. radiatum* is used as a placebo to boost the morale of parturient women?

This present study was conducted in an attempt to answer these questions. It was a synthesis of previous studies focused in part on the acute toxicity of this herbal and the other on the comparative effects of its aqueous leaf extract with oxytocic-like substances known and commonly used in obstetrical practice to stimulate labor. So we carried our interest on some physiological parameters which greatly contribute to the success of the deliveries

LITERATURE REVIEW

Phytochemical analysis, acute toxicity and effects on the electrocardiogram

Konan *et al.* [21] had examined the acute toxicity, the natural bioactive compounds contained in the aqueous leaf extract (ESera) and its actions on the electrocardiogram. They were therefore aimed to confirm the use in traditional medicine for the treatment of cardiovascular diseases and childbirth complications. After the revelation of the phytochemical compounds in *S. radiatum* leaves by general reactions, the determination of LD50 of acute toxicity in mice was achieved after treatment with the aqueous leaf extract (ESera). ESera was administrated intraveinously to the animal via the saphenous vein for ECG registration. The phytochemical analysis revealed the presence of quinones, tannins, alkaloids, sterols, terpens, polyphenols, saponosides and reducing compounds. Short treatments (24 hours) of mice with the leaves aqueous extract gave LD_{50} values of 169.7 ± 15 mg/kg of b.w. and of 184.2 ± 21 mg/kg of b.w., respectively by the method of Miller and Tainter and the method of Dragstedt and Lang. ESera induced negative inotrope and chronotrope actions on the global electric activity of rabbit. In Conclusion: 1. The aqueous leaf extract has a low toxicity which permits its use by populations. 2. As shown by the electrocardiac investigation and the phytochemical study of the leaves, *S. radiatum* could have many pharmacological properties justifying its traditional use to treat many diseases including cardiovascular diseases and childbirth complications.

Uterine smooth muscle contractility

Konan *et al.* [22] reported its uterotonic action. *Sesamum radiatum* is employed in traditional medicine for parturient women to facilitate deliveries. In this study, the effects of the aqueous leaf extract were examined on the contractile activity of uterine smooth muscle isolated from pregnant Wistar rats (19-21 days). The isometric contractile force of the uterine smooth muscle bundles was recorded by using a strain gauge. *S. radiatum* aqueous leaf extracts (ESera, 1×10-4 µg/ml - 100µg/ml) showed uterotonic properties. These uterotonic effects were characterized by the increase of the amplitude, the frequency and the basal tone of the uterine smooth muscle strips in normal Mac Ewen solution and by the development of contracture in depolarizing solution and in solution without calcium. Similar effects were observed with Oxytocin (OT, 2.5×10-14 µg/ml - 2.5×10-9 µg/ml) and misoprostol (Miso, 1×10-3 µg/ml – 0.08 µg/ml). In Ca2+-free solution, the addition of the ESera (10 µg / ml) elicited the development of contracture in the presence of EGTA (0.1 mM). This result suggests that ESera could act on the double calcium flux (intracellular and extracellular) like misoprostol, a synthetic analogue of prostaglandin E1. In conclusion, the aqueous leaf extract of *S. radiatum* (ESera) had uterotonic effects (prostaglandin-like activity) on uterine contraction in pregnant rats.

Arterial blood pressure and cardiovascular system

Konan *et al.* [23] reported the effects on the cardiovascular system. The effects of the aqueous extract of *Sesamum radiatum S*chum. & Thonn. (ESera) were studied on the cardiovascular system of mammalians. ESera administered intravenously (6×10^{-4} g/kg b.w. – 5.7×10^{-2} g/kg b.w.) caused a decrease in the arterial pressure (hypotension) in a dose-dependent manner ($ED_{50} = 1.3 \times 10^{-2}$ g/kg b.w.). These effects induced by ESera were reversed in the presence of atropine at a concentration of 10^{-8} g/kg b.w. Our observations regarding the isolated heart of rat showed that the extract induced both negative inotropic and negative chronotropic effects. Similarly, the experimentation based on the isolated aorta obtained from guinea-pig revealed that the extract decreased the basal tonus of this smooth muscle. These results suggest that ESera could act via cholinergic receptors. The effects of ESera could result from both cardiodepression and vasorelaxation mechanism.

Konan *et al.* [24] have studied the vasorelaxant effect of this herbal. *Sesamum radiatum S*chum. & Thonn (Pedaliaceae) is an annual herbaceous plant, which belongs to the family Pedaliaceae and genus *Sesamum.* Sesame is used in traditional medicine in Africa and Asia for many diseases treatment. Sesame plant especially the leaves, seeds and oil are consumed locally as a staple food by subsistence farmers. The study analyses the relaxation induced by the aqueous extract of leaves from sesame (ESera), compared with those of acetylcholine (Ach) in the guinea-pig aortic preparation (GPAPs), in order to confirm the use in traditional medicine for cardiovascular diseases. The longitudinal strips of aorta of animals were rapidly removed from animals. The aorta was immediately placed in a Mac Ewen solution. Experiments were performed in preparations with intact endothelium as well as in aorta where the endothelium had been removed. The preparations were suspended between two L-shaped stainless steel hooks in a 10 ml organ bath with Mac Ewen solution. The isometric contractile force of the aorta strips of guinea-pig were recorded by using a strain gauge. All both drugs caused concentration-dependent relaxations responses. The aqueous extract of leaves from sesame ESera (1×10^{-7} – 0.1 µg/ml) caused a graded relaxation in GPAPs with intact endothelium, with a EC_{50}-value of 1×10^{-4} µg/ml. The same effect was observed with ACh (7 × 10-2 nM – 7 × 10-1 µM), which caused relaxation in a concentration-dependent manner. The relaxation in response to ESera and, like that to Ach in GPAPs without endothelium, was fully abolished. Destruction of the endothelium or incubation with the nitric oxide synthase inhibitor (L-NNA) significantly enhanced the inhibition of the relaxation response to ESera. Moreover, all concentrations induced vasoconstrictions. However, L-NNA produced a significant displacement to the right (about 65-fold) of the relaxation response to ESera. Similar results were obtained with Ach. Both diclofenac and tetra-ethyl-ammonium (TEA) pre-treatment of GPAPs induced a suppression of the relaxation caused by ESera, and produced a very significant rightward shifts of the CRC (16-fold) for diclofenac and increase the Emax. In contract, the relaxation caused by Ach was not significant affected by diclofenac or by TEA. Thus, the present results indicate clearly that the nitric oxide largely contribute to the relaxation effect of ESera and of Ach in GPAPs. In addition, their contractile effects are also mediated by cyclooxygenase activation, and probably the K^+ channels involvement, that confirm the use of various preparations of ESera for the treatments of cardiovascular diseases.

DISCUSSION AND CONCLUSION

S. radiatum has a low toxicity [21]. The toxicity of *S. radiatum* is observed in sheep but not in humans [16]. This difference is related to the doses and routes of administration. Lethal dose often varies depending on the method of administration, for instance many substances are less toxic when administered orally than when intraperitonially administered. In humans, this plant species undergoes thermal effects during cooking. On the therapeutic level, the doses used by TBAs were lower than those swallowed by sheep. These arguments are consistent with those of Lullman *et al.* [25]. According to these authors, the toxicity of a same extract can change. It depends on several parameters including the extraction method, the administration routes, the doses and individual susceptibilities, *etc.* All pharmacodynamic substances are toxic when administered doses are supraliminal. The toxicity is related to the dose administered. It increases with the dose. Thus, the toxicity of *S. radiatum* can not be a barrier to its use for therapeutic purposes [21]. According to literature, the doses used by people to facilitate childbirth are low justifying the absence of toxicity cases in humans.

S. radiatum aqueous leaf extract was a uterotonic substance. This plant extract increased the rate and amplitude of the uterine contractile activity in normal solution and caused smooth muscle contractions when the uterine smooth muscle bundles were placed in a depolarizing solution. And in the modified calcium-free solution, the addition of *S. radiatum* aqueous leaf extract caused the development of contracture in the presence of EGTA, a specific chelator of calcium ion (Ca^{++}). As misoprostol (Cytotec®), a synthetic analogue of prostaglandin E1, *S. radiatum* aqueous leaf extract mobilized extracellular calcium and intracellular calcium [22]. This fact suggested that *S. radiatum* aqueous leaf extract could act on the double calcium flux. This prostaglandin-like activity was summarized by the ability to mobilize intracellular and extracellular calcium, which confirmed the uterotonic property of *S. radiatum* aqueous leaf extract. These authors also showed that the effects of *S. radiatum* aqueous leaf extract were similar to those of oxytocin (Syntocinon®). The effects of oxytocin had been described by several authors [26-29], while those of misoprostol were described by Hofmeyr *et al.* [30] and Wing *et al.* [31]. Indeed, because of their uterotonic properties, oxytocin and misoprostol were used in obstetrics and gynecology practices to induce and / or facilitate labor [32-37].

The uterotonic action of *S. radiatum* aqueous leaf extract was an asset for its use to facilitate childbirth. According to some authors, uterine contractility plays a crucial role in childbirth. Labor failure is partly due to dysfunction of uterine contraction argued that Ca^{++} mobilization is essential during uterine contraction even if the mechanisms underlying this activity of uterus are not completely understood [29,38-42]. For many authors, the spontaneous onset of parturition is associated with the development of coordinated and rhythmic contractions of the uterine smooth muscle. During childbirth, the uterine contraction is the driving force that allows cervical dilation and fetal growth in the mobile birth canal [1].

S. radiatum aqueous leaf extract induced hypotension as oxytocin (Syntocinon®) and misoprostol (Cytotec®), pharmacodynamic substances commonly used in obstetrics and gynecology [23]. This hypotensive effect of *S. radiatum* leaf extract could justify its use in traditional medicine to facilitate labor in parturient woman [23,24]. Many authors reported that the hypotension induced by oxytocic-like substances would be beneficial for parturient women. It minimizes blood loss due to haemorrhages during the delivery. These haemorrhages complicate 5 % of births and are a leading cause of maternal mortality before the thromboembolic diseases and complications of hypertension [43]. Clinically, the pharmacological management is primarily based on the use of oxytocic-like substances because of their hypotensive property. Misoprostol, a synthetic analogue of prostaglandin E1 (PGE1) is used in the treatment of postpartum haemorrhage resistant to usual oxytocic-like treatments [44,45]. Because of their cardiodepressive and vasorelaxant actions, these substances reduce the cardiac blood flow and blood flow velocity in the vessels. These combined effects could significantly reduce blood loss during the delivery. Thus, *S. radiatum* aqueous leaf extract as oxytocin (Syntocinon®) and misoprostol (Cytotec®) had a hypotensive effect which could minimize the heavy blood loss caused by haemorrhages during childbirth.

To summarize, *S. radiatum* had a low toxicity which does not limit its use for therapeutic purposes. The low doses can be used for therapeutic purposes. In the cardiovascular system and uterine smooth muscle, the effects of its aqueous leaf extract were comparable to those of oxytocin and misoprostol, a synthetic analogue of prostaglandin E1 (PGE1). Oxytocin and prostaglandin E (PGE) were employed in obstetrics and gynecology to induce and / or facilitate labor. These pharmacodynamic substances are used in obstetric practice for two reasons: reduction of blood pressure and uterotonic property. Their uterotonic and hypotensive actions contribute strongly to the success of the deliveries. *S. radiatum* aqueous leaf extract had these two properties. Indeed, this plant extract had a utéronic action and hypotensive effect. These two properties give to *S. radiatum* an interest in human medicine especially in the field of obstetrics and gynecology. *Sesamum radiatum* Schum. & Thonn. (Pedaliaceae) can be used to facilitate childbirth in parturient women.

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COMPETING INTERESTS

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

AUTHORS' CONTRIBUTIONS

All co-authors have contributed to the study design, data search and analysis, and write-up of the manuscript.

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