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FULL PAPER

The antifertility potential of beluntas leaves (pluchea indica): From effects on spermatozoa to phylogenetic analysis of the pluchea genus

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This study investigates the antifertility potential of Beluntas leaves (Pluchea indica) by its comparison with related species within the Pluchea genus through phylogenetic and bioinformatics approaches. By collecting genetic sequence data of Pluchea species from the GenBank NCBI database, analyses were conducted using MEGA X software to generate a phylogenetic tree, amino acid composition, and genetic distance table. Among the 13 Pluchea species analyzed, this research found that P. indica has significant potential as an antifertility agent based on its impact on the quality of male white rat spermatozoa, including motility and spermatogenic cell count. Furthermore, phylogenetic analysis indicates a close genetic relationship between P. indica and P. ovalis, suggesting the potential of P. ovalis as a new antifertility candidate. These results affirm the potential of Beluntas leaves as a male antifertility agent and open opportunities for further research on the potential of other Pluchea species. This study underscores the importance of bioinformatics studies in identifying plants for antifertility drugs, especially within the Pluchea genus, and suggests the need for further laboratory analysis on species closely related to P. indica to verify their antifertility potential.

KEYWORDS

Male Antifertility; Beluntas leaves (Pluchea indica); phylogenetic analysis; bioinformatics; genetic relationship of Pluchea species.

Introduction

In the quest for safe, effective, and widely acceptable contraceptive solutions, research into natural resources, particularly herbal plants, has garnered significant attention. One such plant of interest is Beluntas (Pluchea indica), traditionally used in herbal medicine in several Asian countries [1-5]. Active components in Beluntas leaves, such as tannins, alkaloids, and flavonoids, have shown significant effects in reducing the quality of spermatozoa in preliminary studies [6-10]. This potential opens new avenues in male contraception research, where current options

are still very limited and often come with undesirable side effects. Therefore, a deep understanding of the action mechanisms and effectiveness of Beluntas leaves as an antifertility agent offers promising prospects for a more natural and potentially safer male contraceptive alternative. Figure 1 illustrates the Beluntas plant, showcasing its unique physical characteristics that are not only significant in traditional medicine but also pivotal in scientific research.

Moreover, advancements in bioinformatics technology and phylogenetic analysis [11-15] provide powerful tools for delving deeper into the genetic potential of Pluchea indica and related species within the Pluchea genus [16-20]. Through comparative and phylogenetic analysis, this study not only seeks to confirm the antifertility efficacy of Pluchea indica, but also to identify other species within the genus that may have similar or better potential [21-23]. Thus, this research not only provides new insights into the contraceptive potential of Beluntas leaves, but also opens the possibility of further exploration of biodiversity for the development of innovative and sustainable herbal-based male contraception, overcoming limitations and challenges existing in current male contraceptive methods. Figure 2 details the active components in Beluntas leaves, such as tannins, alkaloids, and flavonoids, which are critical to the plant's antifertility effects. Understanding these compounds is essential for harnessing the contraceptive potential of Pluchea indica, as they are directly responsible for the observed decrease in sperm quality, including motility and viability.

The latest research on antifertility with herbal plants has been widely studied and is developing rapidly [24-26]. In recent developments in male antifertility research, the focus has shifted towards the use of phytopharmaceuticals as a more natural and less side-effect-prone alternative compared to the synthetic contraceptive methods. Research on Pluchea indica, particularly in the context of using its leaves as an antifertility agent, occupies an important place in contemporary scientific literature. New studies highlight the potential of this plant extract in reducing sperm quality, including decreased motility and viability of spermatozoa, indicating its potential as a male contraceptive. Advances in bioinformatics analysis and phylogenetic techniques have broadened our understanding of the molecular mechanisms behind these antifertility effects, not only in Pluchea indica, but also in related species within the Pluchea genus [27-29]. This indicates a growing trend in male antifertility research, where plant-based studies are receiving more attention as potential solutions for developing new contraceptive methods.

However, despite significant progress, current research still faces challenges in identifying and isolating specific active components responsible for antifertility effects, as well as in fully understanding the mechanisms of action at the molecular level [30-31]. In addition, research on the long-term safety and potential side effects of using these plant extracts as male contraceptives remains limited. Recent studies show advances in genetic and phylogenetic analysis to explore the genetic diversity among species within the Pluchea genus, paving the way for identifying new potential sources for the development of antifertility drugs [32-36]. Thus, although research in this field shows great promise, further studies are needed to overcome these obstacles and optimize the potential of phytopharmaceuticals in male contraceptive applications. Figure 3 presents the research highlights on Pluchea indica and its antifertility effects, encapsulating the key findings and potential of Pluchea indica as a viable source for developing new male contraceptive solutions. These highlights include the identification of active components with antifertility effects, the exploration of the plant's genetic makeup for understanding its contraceptive mechanisms, and the ongoing efforts to establish its safety profile for long-term use.

The novelty of this study lies in the application of phylogenetic and bioinformatics analysis in exploring the antifertility potential of Beluntas leaves (Pluchea indica) and related species within the Pluchea genus, which has not been extensively explored in the context of male contraception. This study expands the knowledge base not only by confirming the antifertility effects of P. indica, documented in previous studies, but also by identifying the potential of other species within the Pluchea genus that may have similar or stronger effects. Through this approach, this research opens opportunities to discover new male antifertility candidates from natural sources, offering a safer and more sustainable alternative to currently available synthetic contraceptive methods.

FIGURE 1 Beluntas (Pluchea indica)

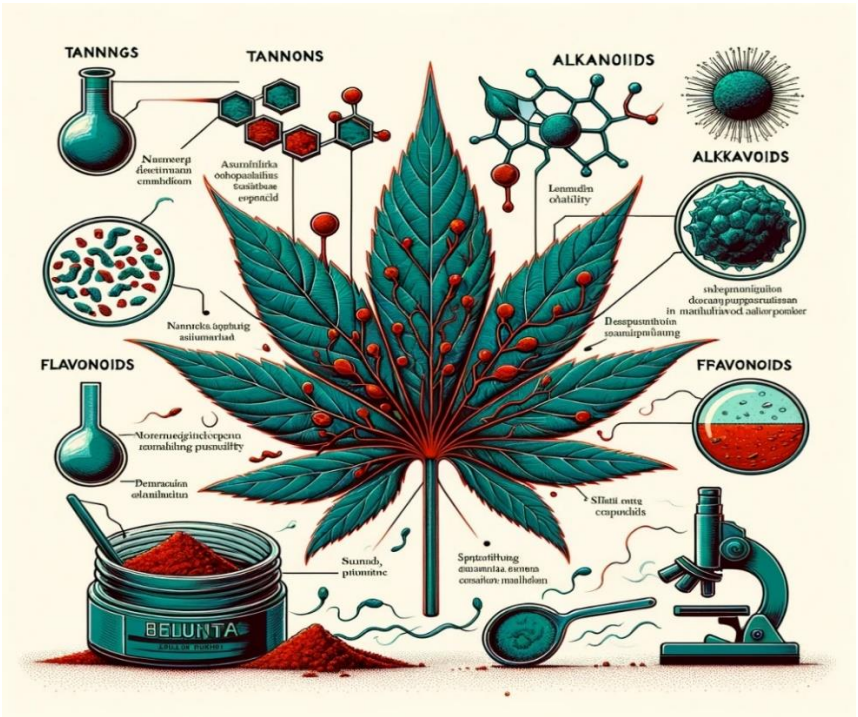

FIGURE 2 Active components in Beluntas leaves

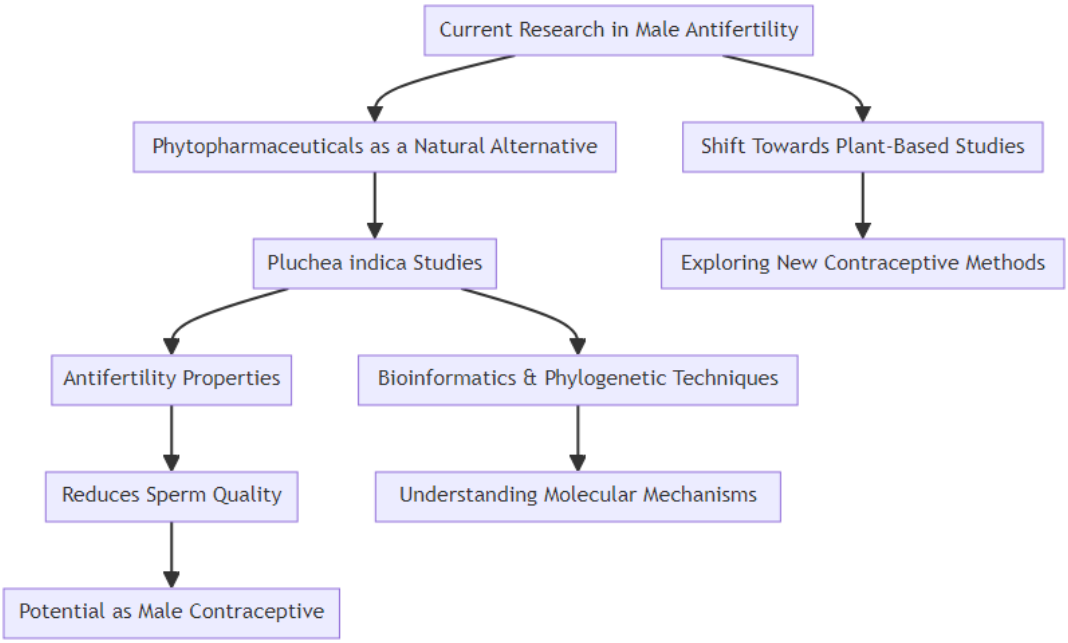

FIGURE 3 The research highlights on Pluchea indica and its antifertility effects

This study significantly contributes to the field of male contraception and phytopharmaceuticals, providing a scientific basis for the development of herbal-based male antifertility drugs. By exploring the genetic relationship between species within the Pluchea genus and characterizing the active components responsible for antifertility effects, this study not only offers new insights into the potential of phytopharmaceuticals in male contraception, but also highlights the importance of genetic diversity in drug development. These results can serve as a reference for further research in the synthesis and formulation of effective and minimally side-effect-prone male antifertility drugs, advancing the fields of pharmacology and male contraception. The objective of this study is to uncover the antifertility potential of Beluntas leaves (Pluchea indica) and related species within the Pluchea genus through phylogenetic and bioinformatics analysis, as a basis for the development of effective and sustainable herbal-based male contraception.

Method

This study method began with the collection of genetic sequence data from species within the Pluchea genus and related species from the Asteraceae family, focusing specifically on Pluchea indica, known to have antifertility potential. These sequences were obtained from the GenBank at the National Center for Biotechnology Information (NCBI) through their website at https://www.ncbi.nlm.nih.gov. Data search was conducted using relevant keywords such as "Pluchea indica", "rbcL gene", and names of species within the Pluchea genus. Once the sequences were obtained, they were downloaded in FASTA format for further analysis. This process ensured that the study was based on a broad and representative dataset, enabling comprehensive research on the antifertility potential of the target species.

Next, phylogenetic and bioinformatics analysis was conducted using MEGA X software (Molecular Evolutionary Genetics Analysis), accessible at https://www.megasoftware.net/. With this software, the collected sequence data were organized and analyzed to construct a phylogenetic tree, showing the evolutionary relationship among species in the Pluchea genus. This analysis involved sequence alignment using the integrated Clustal W tool in MEGA X, followed by the selection of the

most suitable evolutionary model and construction of the phylogenetic tree using the Maximum Likelihood method. The resulting tree provided a graphical visualization of the genetic relationships, allowing the identification of species with high genetic similarity that might have similar or better antifertility potential. Figure 4 outlines the flowchart of the research method, from data collection through NCBI, sequence alignment, and phylogenetic tree construction in MEGA X, to the interpretation of data and analysis of results. This flowchart visually summarizes the step-by-step methodology, illustrating the systematic approach employed in evaluating the antifertility potential of the Pluchea genus.

The final stage of the research method involved interpreting data and analyzing results. Interpretation focused on understanding the phylogenetic relationships revealed through the phylogenetic tree, as well as analyzing amino acid composition to predict biological functions that might be related to antifertility effects. Further analysis of genetic distance among Pluchea species provided insights into the genetic diversity and potential evolution of antifertility features. These analyses were then compared with existing scientific literature to confirm findings and discuss their implications for the development of herbal-based male contraception. Thus, this research method provides a comprehensive approach to evaluating the antifertility potential of the Pluchea genus, significantly contributing to research in herbal contraception.

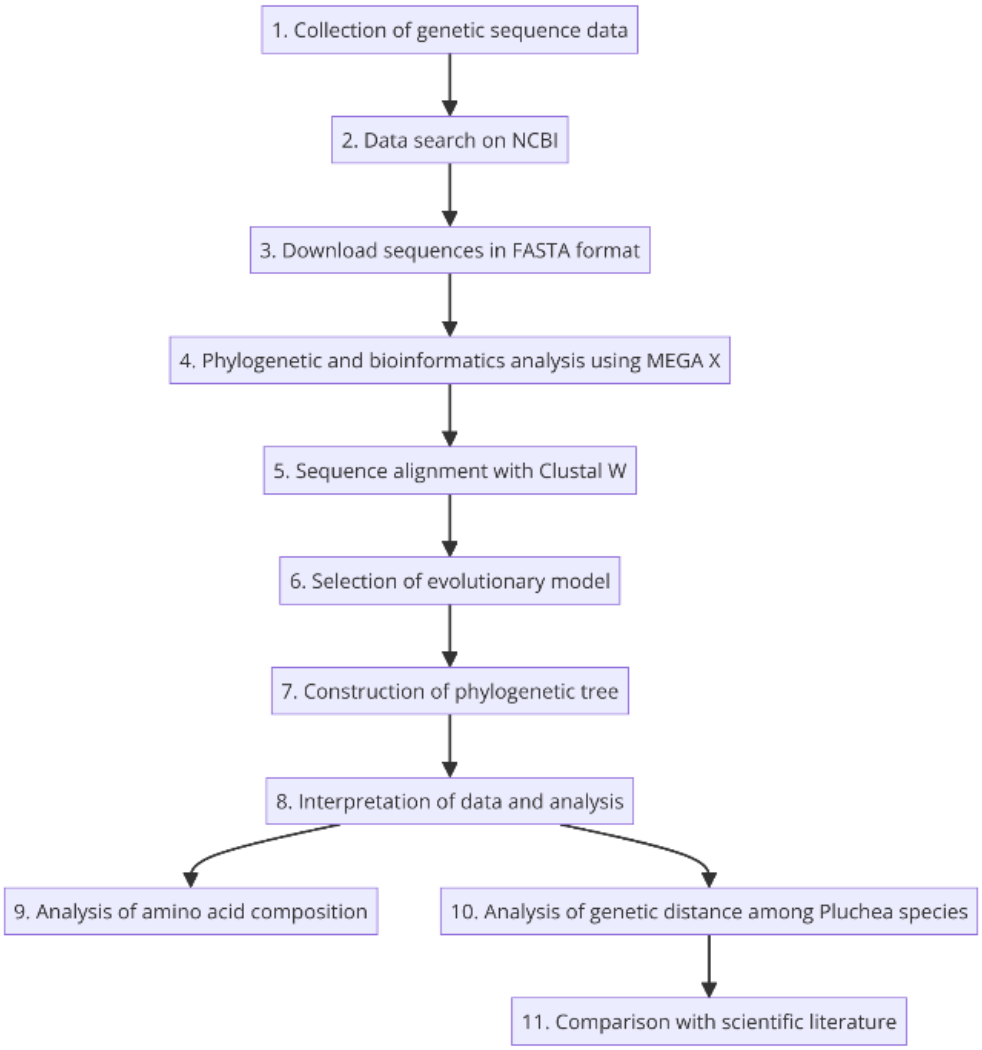

FIGURE 4 Flowchart research

Results and discussion

The analysis in this study, particularly through the use of a phylogenetic tree constructed from genetic sequence data, revealed significant evolutionary relationships between Pluchea indica and related species within the Pluchea genus. The phylogenetic tree results showed that P. indica has a close genetic relationship with several other species in the genus, such as P. ovalis, indicating the possibility that these species may share similar bioactive components responsible for antifertility effects. This analysis provides preliminary evidence of the potential use of other Pluchea species as new sources for the development of herbal-based male contraceptives, expanding the available contraceptive options using genetic diversity within the genus.

The analysis of sample determination based on the completeness of data available in the Gene Bank revealed 13 samples that are members of the Genus Pluchea. These samples include P. sericea, P. sagittalis, P. pteropoda, P. ovalis, P. odorata, P. longifolia, P. lanceolata, P. indica, P. foetida, P. dioscoridis, P. carolinensis, P. camphorate, and P. baccharis. The information obtained from the Gene Bank is presented in Table 1.

TABLE 1 Sample information obtained from the Gene Bank

No.	Species	Gene Bank accession number	Sequence Length (bp)
1.	Pluchea odorata	KJ773762.1	1321
2.	Pluchea longifolia	KJ773761.1	1323
3.	Pluchea foetida	KJ773760.1	1299
4.	Pluchea camphorata	KJ773759.1	1316
5.	Pluchea baccharis	ON341311.1	553
6.	Pluchea carolinensis	KX397901.1	517
7.	Pluchea indica	OK635065.1	570
8.	Pluchea sericea	AY874439.1	1458
9.	Pluchea ovalis	MK285168.1	491
10.	Pluchea dioscoridis	MH234121.1	657
11.	Pluchea pteropoda	NC_060349.1	152300
12.	Pluchea sagittalis	MH049945.1	717
13.	Pluchea lanceolata	KY497911.1	659

Furthermore, the analysis of amino acid composition from the obtained sequences provided essential insights into potential biological functions that could contribute to antifertility activity. Differences in amino acid composition among species could indicate variations in proteins and enzymes involved in reproductive mechanisms, including processes affecting sperm motility and viability [37-39]. Thus, this analysis not only supports the identification of species with high antifertility potential but also aids in understanding the molecular mechanisms underlying these effects. This is crucial for developing antifertility drugs that are not only effective but also have an acceptable safety profile for long-term use.

Recently, the analysis of genetic distance among species in this study provided additional understanding of the level of genetic diversity within the Pluchea genus. This is important for conservation strategies and selecting species for further research in the context of phytopharmaceutical development. By identifying species with relatively close genetic distance to P. indica, this research paves the way for further exploration of those species in the antifertility context. Thus, this analysis not only contributes to the scientific knowledge regarding the antifertility potential of the Pluchea genus, but also supports efforts in developing new, natural, and sustainable male contraceptive drugs (Tables 2 and 3).

TABLE 2 Amino acid composition from the sequence alignment results of 13 sample species from the genus Pluchea

No.	Species	Ala	Cys	Asp	Glu	Phe	Gly	His	Ile	Lys	Leu	Met	Asn	Pro	Gln	Arg	Ser	Thr	Val	Trp	Tyr	Total
1.	*P. sericea*	6,06	2,02	5,05	7,07	7,07	9,09	1,01	3,03	5,05	15,15	1,01	4,04	5,05	4,04	5,05	3,03	7,07	6.06	0,00	4,04	99
2.	*P. sagittalis*	6,06	2,02	5,05	7,07	7,07	9,09	1,01	3,03	5,05	15,15	1,01	4,04	5,05	4,04	5,05	3,03	7,07	6.06	0,00	4,04	99
3.	*P. pteropoda*	2,17	0,00	2,17	4,35	7,61	3,26	2,17	14,13	10,87	6,52	0,00	8,70	3,26	3,26	6,52	3,26	8,70	1,09	2,17	9,78	92
4.	*P. ovalis*	6,06	2,02	5,05	7,07	7,07	9,09	1,01	3,03	5,05	15,15	1,01	4,04	5,05	4,04	5,05	4,04	6,06	6.06	0,00	4,04	99
5.	*P. odorata*	6,06	2,02	5,05	7,07	7,07	9,09	1,01	3,03	5,05	15,15	1,01	4,04	5,05	4,04	5,05	3,03	7,07	6.06	0,00	4,04	99
6.	*P. longifolia*	6,06	2,02	5,05	7,07	7,07	9,09	1,01	3,03	5,05	15,15	1,01	4,04	5,05	4,04	5,05	4,04	6,06	6.06	0,00	4,04	99
7.	*P. lanceolata*	6,06	2,02	5,05	6,06	7,07	9,09	1,01	3,03	5,05	15,15	1,01	4,04	5,05	5,05	5,05	4,04	6,06	6.06	0,00	4,04	99
8.	*P. indica*	6,06	2,02	5,05	7,07	7,07	9,09	1,01	3,03	5,05	15,15	1,01	4,04	5,05	4,04	5,05	3,03	7,07	6.06	0,00	4,04	99
9.	*P. foetida*	0,06	2,02	5,05	7,07	7,07	9,09	1,01	3,03	5,05	8,51	0,00	4,04	5,05	4,04	6,38	7,45	7,07	6.06	0,00	4,04	99
10.	*P. dioscoridis*	4,26	1,06	5,32	3,19	3,19	4,26	8,51	10,64	3,19	15,15	1,01	5,32	4,26	6,38	5,05	3,03	7,45	6,38	1,06	3,19	94
11.	*P. carolinensis*	6,06	2,02	5,05	7,07	7,07	9,09	1,01	3,03	5,05	15,15	1,01	4,04	5,05	4,04	5,05	3,03	7,07	6.06	0,00	4,04	99
12.	*P. camphorata*	6,06	2,02	5,05	7,07	7,07	9,09	1,01	3,03	5,05	15,15	1,01	4,04	5,05	4,04	5,05	3,03	7,07	6.06	0,00	4,04	99
13.	*P. baccharis*	6,06	2,02	5,05	7,07	7,07	9,09	1,01	3,03	5,05	15,15	1,01	4,04	5,05	4,04	5,05	3,03	7,07	6.06	0,00	4,04	99
	Rata-rata	5,65	1,80	4,86	6,51	6,82	8,31	1,65	4,39	5,33	14,04	0,86	4,04	4,86	4,24	5,25	3,61	6,98	5,73	0,24	4,39	98,1

The interpretation of the results of this study indicates that the Pluchea genus, particularly Pluchea indica, holds significant potential as a natural source of antifertility for men. Through phylogenetic and bioinformatics analysis, this study identified close genetic relationships between P. indica and related species, suggesting that the antifertility mechanisms found in P. indica might also be present in other species within the genus. This finding is important as it opens the possibility for the development of new herbal contraceptives that can offer an alternative for men seeking non-hormonal and minimal side-effect contraceptive methods. By expanding our understanding of the antifertility potential of Pluchea species, this research provides a strong foundation for further research in the development of plant-based phytopharmaceuticals.

Moreover, the data interpretation highlights the importance of analyzing amino acid composition and genetic distance in understanding species variations and their bioactive potential. This analysis indicates that variations at the amino acid level can provide insights into the protein functions contributing to antifertility effects, offering a new direction for research into the action mechanisms at the molecular level. This is not only relevant for the development of antifertility drugs but also for a broader understanding of the biological processes affecting fertility. Thus, these findings emphasize the importance of a multidisciplinary approach in phytopharmaceutical research, combining knowledge of genetics, biochemistry, and pharmacology.

In conclusion, this study makes a significant contribution to the literature on herbal contraception and male antifertility. By identifying and analyzing the antifertility potential of Pluchea indica and related species, this study not only adds to our understanding of the bioactive diversity within the Pluchea genus, but also offers a new perspective for the development of innovative male contraceptives. These results encourage further investigation and the development of drug formulations based on natural principles, supporting the search for safer, effective, and user-friendly contraceptive options.

TABLE 3 Results of the genetic distance analysis

	1	2	3	4	5	6	7	8	9	10	11	12	13
Pluchea sericea													
Pluchea sagittalis	0,00												
Pluchea pteropoda	1,90	1,90											
Pluchea ovalis	0,00	0,00	1,88										
Pluchea odorata	0,00	0,00	1,90	0,00									
Pluchea longifolia	0,00	0,00	1,90	0,00	0,00								
Pluchea lanceolata	0,01	0,01	1,90	0,00	0,01	0,01							
Pluchea indica	0,01	0,01	1,90	0,00	0,01	0,01	0,01						
Pluchea foetida	0,00	0,00	1,90	0,00	0,00	0,00	0,01	0,01					
Pluchea dioscoridis	2,72	2,72	1,68	2,67	2,72	2,72	2,72	2,72	2,72				
Pluchea carolinensis	0,00	0,00	1,90	0,00	0,00	0,00	0,01	0,01	0,00	2,72			
Pluchea camphorata	0,00	0,00	1,90	0,00	0,00	0,00	0,01	0,01	0,00	2,72	0,00		
Pluchea baccharis	0,00	0,00	1,90	0,00	0,00	0,00	0,01	0,01	0,00	2,72	0,00	0,00	

Notes:
1 = *Pluchea sericea*
2 = *Pluchea sagittalis*
3 = *Pluchea pteropoda*
4 = *Pluchea ovalis*
5 = *Pluchea odorata*
6 = *Pluchea longifolia*
7 = Pluchea lanceolata
8 = *Pluchea indica*
9 = *Pluchea foetida*
10 = *Pluchea dioscoridis*
11 = *Pluchea carolinensis*
12 = *Pluchea camphorata*
13 = *Pluchea baccharis*

From the perspective of male contraceptive development, this research offers an intriguing contribution compared to conventional approaches that largely focus on hormonal or mechanical methods such as condoms and vasectomy. Herbal contraception, particularly through the use of Pluchea indica, promises a more natural alternative with potentially lower side effects. While hormonal contraception can be associated with mood changes, weight gain, and libido, as well as long-term health risks, the use of plant extracts like P. indica may reduce these risks, offering a solution more in line with healthy lifestyles and individual preferences. However, compared to the direct effectiveness of conventional methods, the main challenge for plant-based contraception lies in ensuring consistent effects, precise dosing, and comprehensive clinical validation to ensure safety and efficacy.

In the context of phytopharmaceutical research, the approach taken in this research-combining phylogenetic and bioinformatics analysis-represents a paradigm shift from direct experimental research to the exploration of genetic and molecular data. This allows for the quick and efficient identification of species with bioactive potential without the need for extensive initial laboratory testing. Compared to other phytopharmaceutical studies that may rely more on trial-and-error for compound screening, this method offers higher efficiency and can direct resources towards the most promising candidates. However, the challenge that arises is the need for strong experimental validation to confirm bioinformatics predictions, ensuring that theoretical findings can be translated into practical applications.

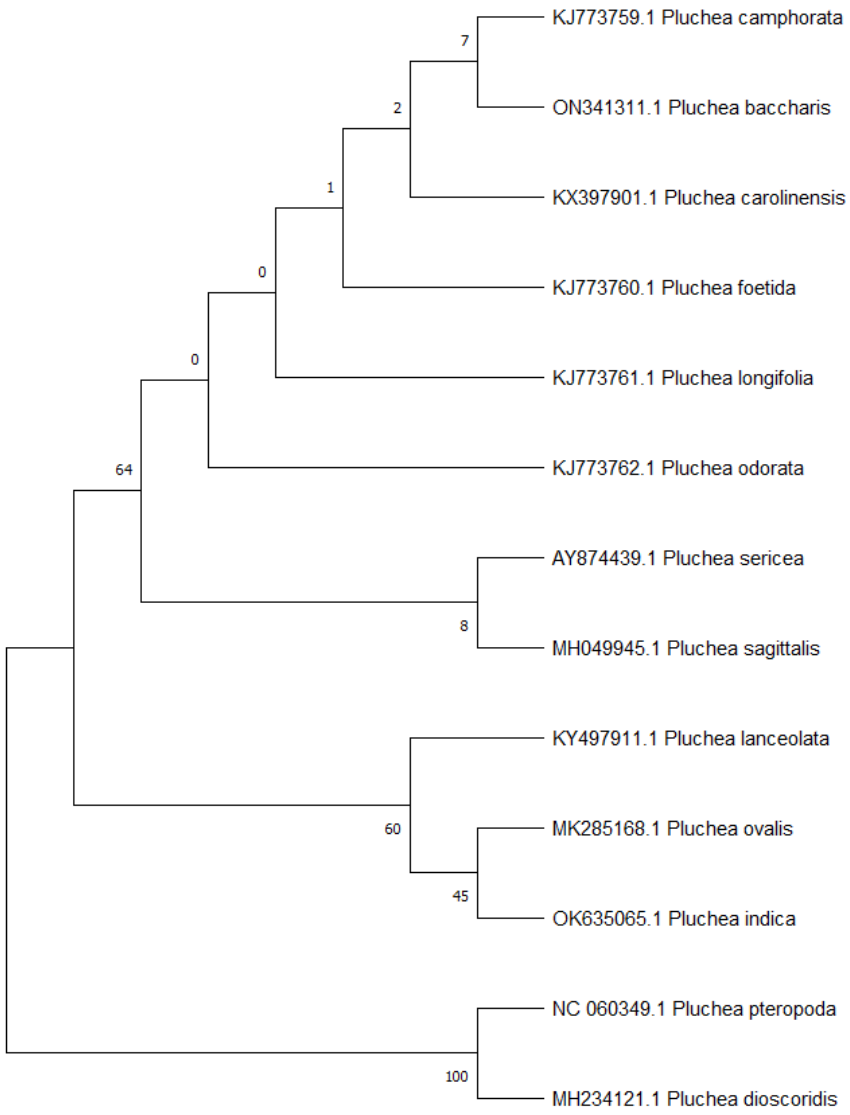

FIGURE 5 Phylogenetic tree results based on sequence alignment and genetic distance analysis

From the perspective of genetic diversity and conservation, this research highlights the importance of understanding genetic variation in species conservation and sustainable use of natural resources. Compared to studies that may focus on a single species without considering its phylogenetic relationships, this study adds a new dimension in evaluating antifertility potential by concerning genetic diversity within the Pluchea genus. This not only has the potential to identify new sources for drug development but also supports conservation efforts by highlighting species that might be important from a biomedical standpoint. However, this also poses the challenge of balancing the exploration of natural resources with the need to ensure sustainable and ethical utilization, preventing overexploitation that could threaten the survival of those species. Figure 5 displays the phylogenetic tree results based on sequence alignment and genetic distance analysis, illustrating the evolutionary relationships among species within the Pluchea genus. This visual representation serves as a crucial tool in understanding the genetic diversity and relatedness of species, guiding the selection of potential candidates for further antifertility research. It underscores the methodological rigor of this study, which integrates

phylogenetic analysis to inform both conservation strategies and the search for effective natural compounds for male contraception, thus ensuring a responsible approach to biodiversity exploration and pharmaceutical development.

Conclusion

This study offers valuable insights into the potential of Pluchea indica and related species within the Pluchea genus as natural sources of male antifertility, highlighting possible alternatives to conventional contraceptive methods that are safer and herbal-based. Through the application of phylogenetic and bioinformatics analysis, this study not only successfully identified genetic relationships that support further research into the bioactive components of these species, but also opened the path for further exploration of genetic diversity in the search for new contraceptive solutions. In conclusion, this study adds to the existing literature by offering an innovative approach in the development of male contraception, while also emphasizing the importance of sustainability and conservation in the use of natural resources for medical purposes.

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Authors' Contributions

- Eko Susetyarini conceptualized the study, led the research design, and contributed to the writing and revision of the manuscript.
- Tutut Indria Permana contributed to the collection and analysis of genetic sequence data and played a pivotal role in the bioinformatics analysis.
- Supiana Dian Nurtjahyani was responsible for the phylogenetic analysis and contributed to the interpretation of data.
- Rahadian Zainul coordinated the research activities, contributed to the study design, data analysis, and was the primary author of the manuscript.
- Vikash Jakhmola contributed to the manuscript's revision and provided critical feedback on the research findings.
- Meksim Rebezov was involved in the analysis of amino acid composition and played a key role in the discussion of the potential biological functions related to antifertility effects.
- Herland Satriawanh provided expertise in genetic distance analysis and contributed to the final interpretation of the study's results.

All authors read and approved the final manuscript.

Conflict of Interest

The authors declare no conflict of interest. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, or in the decision to publish the results.

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References

[1] N. Habibah, H.S.W. Nugroho, I.G.A.S. Dhyanaputri, I.G.A.A. Dharmawati, I.B.O. Suyasa, Phytochemical profile and bioactive compounds of beluntas leaves extract (Pluchea indica L.) and its hydrogel preparations, *Journal of Medical Pharmaceuticaland Allied Sciences*, **2023**, *12*, 6184-90. [Crossref], [Google Scholar], [Publisher]

[2] E.W.C., Ng, Y.K. Chan, S.K. Wong, H.T. Chan, Pluchea indica: An updated review of its botany, uses, bioactive compounds and pharmacological properties, *Pharmaceutical Sciences Asia*, **2022**, *49*. [Crossref], [Google Scholar], [Publisher]

[3] N.P.E. Hikmawanti, F.C. Saputri, A. Yanuar, I. Jantan, R.A. Ningrum, A. Mun'im, Insights into the anti-infective effects of Pluchea indica (L.) less and its bioactive metabolites against various bacteria, fungi, viruses, and parasites, *Journal of Ethnopharmacology*, **2023**, 117387. [Crossref], [Google Scholar], [Publisher]

[4] A. Sabrina, Z.P. Aminullah, Presenting local cultural knowledge as a bridge to aid students' comprehension in identification and classification: the case of cassumunar ginger (Zingiber purpureum) and marsh fleabean (Pluchea indica), In *Journal of Physics: Conference Series*, IOP Publishing, **2020**, *1440*, 12071 [Crossref], [Google Scholar], [Publisher]

[5] S.R. Ibrahim, A.A. Bagalagel, R.M. Diri, A.O. Noor, H.T. Bakhsh, G.A. Mohamed, Phytoconstituents and pharmacological activities of Indian Camphorweed (Pluchea Indica): A multi-potential medicinal plant of nutritional and ethnomedicinal importance, *Molecules*, **2022**, *27*, 2383. [Crossref], [Google Scholar], [Publisher]

[6] S. Bahri, A. Lestari, V.M. Devi, B.F. Rahmayanti, M.A. Rosyidi, Effect of beluntas leaf (Pluchea indica) ethanol extract on mortality of instar II larvas (Spodoptera litura F.) on long bean plant (Vigna sinensis L.), *Jurnal Pijar Mipa*, 2022, *17*, 538-543. [Google Scholar], [Publisher]

[7] N. Habibah, H.S.W. Nugroho, I.G.A.S. Dhyanaputri, I.G.A.A. Dharmawati, I.B.O. Suyasa, Phytochemical profile and bioactive compounds of beluntas leaves extract (Pluchea indica L.) and its hydrogel preparations, *Journal of Medical Pharmaceuticaland Allied Sciences*, **2023**, *12*, 6184-90. [Crossref], [Google Scholar], [Publisher]

[8] W. Adiwijaya, R. Setiadhi, V.K. Sugiaman, Antibacterial potential ethanol extract of beluntas leaves (Pluchea indica L) to Streptococcus sanguinis, *Journal of Syiah Kuala Dentistry Society*, **2022**, *7*, 78-85. [Google Scholar], [Publisher]

[9] M. Martina, T. Regina, N.N. Sumerti, Ability difference of Beluntas Leaf (Pluchea indica L) ethanol extract and avocado leaf (Persea americana Mill) ethanol extract in inhibitingcaries-causing streptococcus mutansbacteria, **2019**. [Crossref], [Google Scholar], [Publisher]

[10] D. Sylvana, M. Amir, C.B. Purnamasari, A. Iskandar, V. Asfirizal, Antibacterial activity of ethanol extract of Beluntas leaves on Streptococcus mutans, Porphyromonas gingivalis, and Enterococcus faecalis, *Padjadjaran Journal of Dentistry*, **2021**, *33*, 191-198. [Google Scholar], [Publisher]

[11] A. Ansori, R. Zainul, In Silico B-Cell Epitope vaccine design and phylogenetic analysis of ebola virus envelope glycoprotein, *Indonesian Journal of Pharmacy*, **2023**. [Google Scholar], [Publisher]

[12] V.D. Kharisma, A.N.M. Ansori, M.E. Ullah, T.G.A. Dings, R.T. Probojati, A. Fadholly, D.D.R. Turista, M.R. Tacharina, R. Zainul, A bioinformatics approach to design a novel epitope-based vaccine against Simian Immunodeficiency Virus (Retroviridae: Lentivirus), *Genbinesia Journal of Biology*, **2022**, *2*, 16-22. [Crossref], [Google Scholar], [Publisher]

[13] V.D. Kharisma, A.N.M. Ansori, V. Jakhmola, W.C. Rizky, M.H. Widyananda, R.T. Probojati, A.A.A. Murtadlo, M. Rebezov, P. Scherbakov, P. Burkov, Y. Matrosova, A. Romanov, M.A.E.M. Sihombing, Y. Antonius, R. Zainul, Multi-strain human papillomavirus (HPV) vaccine innovation via computational study: A mini review, *Research Journal of Pharmacy and Technology*, **2022**, *15*, 3802-3807. [Crossref], [Google Scholar], [Publisher]

[14] D.D.R. Turista, V.D. Kharisma, A.N.M. Ansori, K.A. Kardanova, I.R. Aslanov, I.M. Dotkulov, A.Z. Apshev, A.A. Dokshukin, M. Rebezov, V. Jakhmola, E. Md. Ullah, R. Zainul, Antiviral investigation of cassia alata L. bioactive compounds for SARS-CoV-2 Mpro: In Silico approach, *Research Journal of Pharmacy and Technology*, **2023**, *16*, 5610-5616. [Crossref], [Google Scholar], [Publisher]

[15] N.S. Aini, A.N.M. Ansori, V.D. Kharisma, M.F. Syadzha, M.H. Widyananda, A.A.A. Murtadlo, R.T. Probojati, Md. E. Ullah, S.W. Naw, V. Jakhmola, R. Zainul, Potential roles of purslane (Portulaca oleracea L.) as antimetabolic syndrome: a review, *Pharmacognosy Journal*, **2022**, *14*, 710-714. [Crossref], [Google Scholar], [Publisher]

[16] D.K. Wahyuni, S.R. Mukarromah, P. Rakhmad, M. Ilham, G.A. Rakashiwi, D.T. Indriati, B.F. Yoku, H. Purnobasuki, J. Junairiah, S. Prasongsuk, Morpho-anatomical characterization and DNA barcoding analysis of Pluchea indica (L.) Less, *Biodiversitas Journal of Biological Diversity*, **2023**, *23*. [Crossref], [Google Scholar], [Publisher]

[17] Y. Lin, A.K. Banerjee, H. Wu, F. Tan, H. Feng, G. Tan, W. Guo, Y. Huang, Prominent genetic structure across native and introduced ranges of Pluchea indica, a mangrove associate, as revealed by microsatellite markers, *Journal of Plant Ecology*, **2020**, *13*, 341-353. [Google Scholar], [Publisher]

[18] J. Luo, X. Liu, T. Li, H. Chen, T. Qu, Y. Wang, S. Yu, Z. Fu, Characterization and phylogenetic analysis of the chloroplast genome of Duhaldea cappa (Buch.-Ham. ex D. Don) Pruski & Anderb.(Asteraceae), *Mitochondrial DNA Part B*, **2024**, *9*, 186-190. [Crossref], [Google Scholar], [Publisher]

[19] A.A. Naranjo, R.R. Pathirickal, K.N. Gandhi, P.G. Delprete, R.M. Baldini, A. Santos-Guerra, L. Sánchez-Pinto, J. Francisco-Ortega, Honoring Sabin Berthelot: Nomenclature and botanical history of Berthelotia DC.(Asteraceae, Inuleae), *Webbia*, **2022**, *77*, 207-228. [Google Scholar], [Publisher]

[20] Z. Zhou, T. Pu, B. Duan, M. Zhang, Phylogenetic relationship and characterization of the complete chloroplast genome of Laggera crispata, a folk herbal medicine plant in China, *Mitochondrial DNA Part B*, **2022**, *7*, 1148-1150. [Crossref], [Google Scholar], [Publisher]

[21] N. Fatima, S.S.R. Baqri, A. Alsulimani, S. Fagoonee, P. Slama, K.K. Kesari, S. Roychoudhury, S. Haque, Phytochemicals from Indian ethnomedicines, **2021**. [Crossref], [Google Scholar], [Publisher]

[22] W. Zaman, M. Ahmad, M. Zafar, H. Amina, F. Ullah, S. Bahadur, A. Ayaz, S. Saqib, N. Begum, S. Jahan, The quest for some novel antifertility herbals used as male contraceptives in district Shangla, Pakistan, *Acta Ecologica Sinica*, **2020**, *40*, 102-112. [Crossref], [Google Scholar], [Publisher]

[23] W. Zaman, M. Ahmad, M. Zafar, H. Amina, S. Saqib, F. Ullah, A. Ayaz, S. Bahadur, S. Park, Diversity of medicinal plants used as male contraceptives: An initiative towards herbal

contraceptives, **2022**. [Google Scholar], [Publisher]
[24] N.S. Aini, V.D. Kharisma, A. Ansori, A.A.A. Murtadlo, M.B. Tamam, D.D.R. Turista, I. Rosadi, T.H. Sucipto, V. Jakhmola, M. Rebezov, E. Ullah, R. Zainul, Bioactive compounds screening of Rafflessia sp. and Sapria sp.(Family: Rafflesiaceae) as anti-SARS-CoV-2 via tetra inhibitors: An in silico research, *Journal of Pharmacy and Pharmacognosy Research*, **2023**, *11*, 611-624. [Crossref], [Google Scholar], [Publisher]
[25] A.N.M Ansori, A.A.A. Murtadlo, V.D. Kharisma, B. Muchtaromah, M.B. Tamam, D.D.R. Turista, I. Rosadi, V. Jakhmola, M. Rebezov, R. Zainul, Alpha-mangostin as an antiviral candidate: A mini review, *Journal of Medicinal and Chemical Sciences*, **2024**, *7*, 275-286. [Crossref], [Pdf], [Publisher]
[26] Y. Ale, S. Rana, N. Nainwal, S. Rawat, M. Butola, R. Zainul, V. Jakhmola, Phytochemical screening and green synthesis of antibacterial silver nanoparticles of sapindus mukorossi fruit extracts, *Research Journal of Pharmacy and Technology*, **2023**, *16*, 5643-5649. [Crossref], [Google Scholar], [Publisher]
[27] E.W. Sukarjati, I.A. Pramusinta, A. Rahayu, Potential Extract of Lerak Fruit (Sapindus Rarak), Pegagan (Centella Asiatica,) Mimba Seed (Azadirachta Indica A. Juss) and Mixing of Third Extract to Motility and Viability of Spermatozoa Guinea Pigs (Cavia Porcellus), *International Journal of Health & Medical Research*, **2023**, *2*,141-146. [Crossref], [Google Scholar], [Publisher]
[28] M. Kanedi, Indonesian medicinal plants that have the potential to affect testicular function: A Review. *GSC Advanced Research and Reviews*, 2023, *14*, 163-172. [Google Scholar], [Publisher]
[29] H. Setiawan, S.W. Wulandari, E.D. Agustina, Antispermatogenic activity of ethanolic extract of Calina papaya leaves on seminiferous tubules Wistar rats. Jurnal Kedokteran Hewan-Indonesian Journal of Veterinary Sciences, **2021**, *15*, 21-26. [Crossref], [Google Scholar], [Publisher]
[30] E. Tvrdá, F. Benko, T. Slanina, S.S. du Plessis, The role of selected natural biomolecules in sperm production and functionality, *Molecules*, **2021**, *26*(17), p.5196. [Crossref], [Google Scholar], [Publisher]
[31] S.S. Ramgir, K. Renu, B. Vellingiri, A. George, D. Tirupapuliyur, P. Thiagarajan, A. Valsala Gopalakrishnan, Phytomedicinal therapeutics for male infertility: critical insights and scientific updates, *Journal of Natural Medicines*, **2022**, *76*, 546-573. [Google Scholar], [Publisher]
[32] Z. Liang, X. Xie, Y. Liang, H. Zhang, W. Zhao, L. Tang, Z. Chao, The complete chloroplast genome of Pluchea pteropoda Hemsl, a mangrove associate plant, *Mitochondrial DNA Part B*, **2021**, *6*, 1729-1731. [Crossref], [Google Scholar], [Publisher]
[33] X. He, S. Dong, C. Gao, Q. Wang, M. Zhou, R. Cheng, The complete chloroplast genome of Carpesium abrotanoides L.(Asteraceae): Structural organization, comparative analysis, mutational hotspots and phylogenetic implications within the tribe Inuleae, *Biologia*, **2022**, *77*, 1861-1876. [Google Scholar], [Publisher]
[34] X. Shi, W. Xu, M. Wan, Q. Sun, Q. Chen, C. Zhao, K. Sun, Y. Shu, Comparative analysis of chloroplast genomes of three medicinal Carpesium species: Genome structures and phylogenetic relationships, *PLoS One*, **2022**, *17*, 272563. [Crossref], [Google Scholar], [Publisher]
[35] P. Poczai, Comparative plastome analysis of Blumea, with implications for genome evolution and phylogeny of Asteroideae, **2021**. [Google Scholar], [Publisher]
[36] L. Yuan, Y. Ni, J. Li, H. Yang, J. Yue, X. Zhang, H. Chen, C. Liu, The complete chloroplast genome of Inula britannica and the phylogeny and evolution of the genus Inula, **2023**. [Google Scholar], [Publisher]
[37] A. Agarwal, M.K. Panner Selvam, S. Baskaran, Proteomic analyses of human sperm cells: understanding the role of proteins and molecular pathways affecting male reproductive health, *International Journal of*

Molecular Sciences, **2020**, *21*, 1621. [Crossref], [Google Scholar], [Publisher]

[38] M.R. Ugur, T. Dinh, M. Hitit, A. Kaya, E. Topper, B. Didion, E. Memili, Amino acids of seminal plasma associated with freezability of bull sperm, *Frontiers in Cell and Developmental Biology*, **2020**, *7*, 347. [Crossref], [Google Scholar], [Publisher]

[39] J. Santiago-Moreno, E. Blesbois, Functional aspects of seminal plasma in bird reproduction. *International Journal of Molecular Sciences*, **2020**, *21*, 5664. [Crossref], [Google Scholar], [Publisher]

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