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Typhonium flagelliforme as a Cancer Prevention Plant-Based on In Vitro, In Vivo and Bioinformatics Research Method: A Systematic Literature Review

Teddy Siswanto[1]*, Ratna Shofiati[2], Ismi Hasnatul Afifah[1]

[1]Information System, Trisakti University
[2]Informatics, Trisakti University

*Corresponding author:
E-mail:
teddysiswanto@trisakti.ac.id

ABSTRACT

The development of cancer-preventing plant research develops along with the development of science and information technology. The purpose of this study was to collect research related to the *Typhonium flagelliforme* plant so that it can be used to add to the research literature that synergizes with multi-scientific disciplines. This research method uses a Study Literature Review from the journals Proquest, ScienceDirect, NCBI, and other journals since 2012 with the keywords *Typhonium flagelliforme* or Rodent Tuber or *Keladi-tikus* to identify the type of research In Vitro, In Vivo and Bioinformatics and search by journal publisher category. The results of the Systematic Literature Review research obtained a total of 194 papers and after being traced from the abstract, then 51 papers were selected consisting of 42 In Vitro research papers, 1 In Vivo paper and 6 Bioinformatics papers, and a combination of In Vitro and In Vivo papers totaling 2 papers. Meanwhile, based on scientific fields the most are from Natural Science, Medicine, Bioinformatics, and Pharmacy. Based on the results of research identification, further research is proposed for *Typhonium flagelliforme* as a plant that has the potential to prevent cancer, can involve researchers from different scientific families so that it is suitable for multi-disciplinary research by synergizing the three methods of In Vitro, In Vivo and Bioinformatics through the involvement of researchers from Biology, Chemistry, Medicine, Pharmacy and Informatics to get further research depth.

Keywords: Typhonium flagelliforme, systematic literature review, in vitro, in vivo, bioinformatics

Introduction

The development of cells that are resistant to several substances is one of the problems why cancer treatment is not completely successful. Herbs use natural ingredients in the treatment of cancer so hopefully, they will not give side effects. Natural ingredients that are used are widely grown in Indonesia. One of the plants that have the potential to have medicinal properties to prevent cancer is the *Keladi-tikus* plant. Research on alternative medicine with Rodent Tuber or *Typhonium flagelliforme* Lodd has been carried out in several countries by researchers. Research conducted on *Keladi-tikus* plants was carried out using In-Vitro, In-Vivo, and Bioinformatics methods. In vitro research is carried out in a controlled environment outside of living organisms, in a glass vessel, including propagating plants utilizing plant tissue culture through modification of plant genotypes, producing biomass and secondary metabolites, followed by research to see the content of compounds that have the potential to become superior medicinal ingredients. In-Vivo research, tests are carried out in living organisms to see the reactions of a given trial result. This research is not to find a gap analysis of the three methods of In Vitro, In Vivo, and Bioinformatics,

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but all three methods can synergize with each other to increase the accuracy of research results through literature enrichment. In Vivo research will prove the effects of the compounds tested on animals and even humans to ensure the success or failure of the research. In Vitro Research has the characteristics of tight control on the chemical and physical environment, higher throughput, relatively low cost, and does not use animal testing. However, In Vitro has a substantial drawback namely that the replication conditions of isolated and cultured primary cells are usually very different from that of the cell types in a living organism. While Bioinformatics research is a basic DNA research that includes the basic elements Adenine, Adenine, Cytosine, Guanine, Thymine which can affect the initial process of the In Vitro method through PCR (Polymerase Chain Reaction) with the formation amplification of DNA Primer Design.

Material and Methods

This research is a Systematic Literature Review of *Typhonium flagelliforme* or Rodent Tuber or Keladi-tikus research using In Vitro, In Vivo and Bioinformatics methods. In Vitro and In Vivo method research journal papers were searched through the Journal of Proquest and ScienceDirect in the last 10 years (2012), the Bioinformatics method was through the NCBI website domain and other journals to meet the number of literature studies. The stages in the research methodology include the Search Strategy and Data Extraction.

Search strategy

The process of search strategy by keyword *Typhonium flagelliforme* or Rodent Tuber or *Keladi-tikus* for journals through Proquest resulted in 81 published papers, through Science Direct published 52 published papers, and through NCBI resulted in 38 papers DNA and other journals obtained 24 papers by keywords search. So, the total is 194 papers as shown in figure 1.

Papers that fall into the search category will be saved as Candidate Studies. Furthermore, the process of filtering papers based on abstracts is carried out according to the keyword search category. When the paper matches the research question, it is categorized as a Selected Study. To validate the selected paper, the following procedure is carried out:

- Paper-based on the date of the publication since 2012, but specifically for the NCBI source but due to data limitations, all FASTA data were entered for further processing.
- All publications in the form of journals and conferences are written in full according to citation on reference, especially for some sources in NCBI that do not publish, only their identities can be written.
- Papers from the same source will be sorted from the Systematic Literature Review.

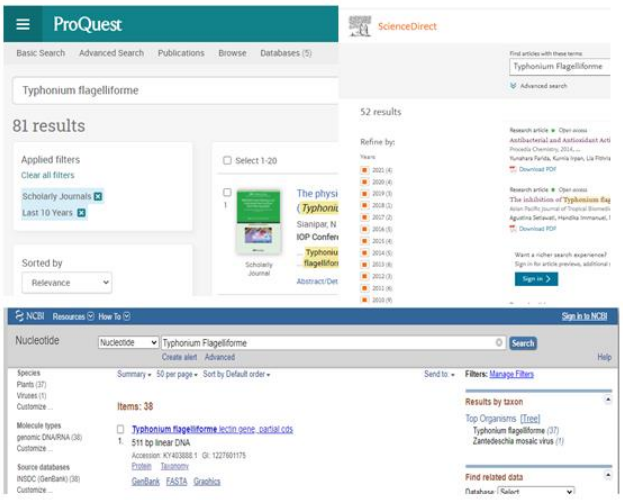

Figure 1. Screenshots search strategy for *Typhonium flagelliforme*

Study selection

Based on the keyword search for the object of research, 194 papers were obtained that matches the 3 words search criteria, 51 papers are included in the candidates for deeper research on the abstract according to the research keyword. After going through a further research process, the following papers were selected as shown in table 1.

Table 1. Abstract according in inclusion criteria

Source	Found	Candidate	Selected
Science Direct	52	9	7
Proquest	81	11	11
NCBI	38	37	9
Others	24	24	24
Total	194	80	51

Data extraction and analysis

Based on the contents of the abstract, processed data, and conclusions, the data extraction will produce similarities and important aspects in research results, then an analysis is carried out for the similarities of the research material carried out, as shown in table 2 count column.

Table 2. Similarities and important aspects in research results

No	Aspect	Sum
1	Using a Random Amplified Polymorphic DNA (RAPD) marker (Lee et al., 2015; Moon et al., 2016; Sianipar et al., 2015a; Sianipar et al., 2015b; Sianipar et al., 2017; Pa. T. Lunwongsa et al., 2018; Putra et al., 2020; Singh & Tripathi, 2018; Farida et al., 2014)	9
2	*Typhonium flagelliforme* has a low genetic early growth ability (sianipar et al., 2015a; Sianipar et al., 2013; Sianipar et al., 2015b, Nesti et al., 2020; Nesti et al., 2021; Inani et al., 2017).	6
3	Anti-cancer compound lectins (Alfarabi et al, 2017; Purnamaningsih et al., 2018), Etil asetat, n-butanol (Zhang et al., 2015), ethanol (Sianipar et al., 2017).	4
4	Analyze comparative DNA barcode sequences (Moon et al., 2016; Chen & Luo, 2012).	2
5	The research method uses apoptosis, is a biological mechanism used by multi-cellular organisms to get rid of cells that don't longer needed by body (Mohd et al., 2014; Purnamaningsih & Sianipar, 2018)	2
6	DNA sequence FASTA file sustainability (Alfarabi et al., 2017; Sousa et al., 2014; Moon et al., 2016; Chen & luo, 2012; Fatima & Yee, 2014; Tajuddin et al., 2013; Lee et al., 2016; Zhang et al., 2015).	8
7	Research combination method I-Vitro dan In-Vivo (Nurrochmad et al., 2015; Graudejus et al., 2019).	2

Results and Discussion

Based on 51 papers that meet the requirements of the search strategy obtained research using the In-Vitro method is 42 papers, In-Vivo is 1 paper, a combination of In-Vitro and In-Vivo totaling 2 papers and Bioinformatics is 6 papers. Although the number of combinations of In Vitro and In Vivo methods is still small, researchers want to prove in real terms how they're In Vitro research results in living organisms. While the results of In Vitro research are very dependent on the PCR used in trials, for that it is necessary to consider a combination of Bioinformatics research, In Vitro to produce a more accurate PCR in the DNA amplification process, the sequence being

studied is then tested in the In Vivo method and the results are analyzed through the marker, as shown in figure 2.

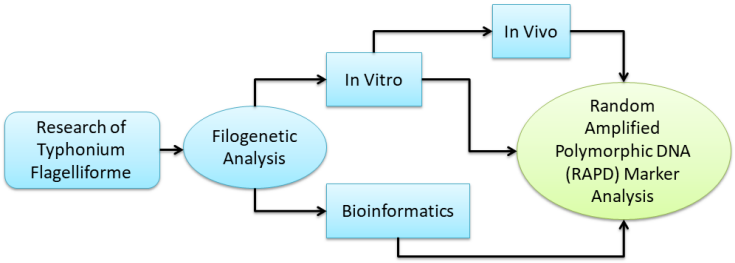

Figure 2. The flow of research synergy on *Typhonium flagelliforme*

Typhonium flagelliforme research began with phylogenetic analysis to determine the value of these plant relationships. The research was continued with In Vitro plant breeding to obtain better potential compounds from the previous generation. Proving the potential of real plants is done through In Vivo research through trials on living things. Bioinformatics research through DNA / RNA / Protein structure analysis will be matched with In Vitro and In Vivo research through RAPD marker analysis.

Based on Scientific Field: Agricultural 3 papers, Biochemistry 1 paper, Bioinformatics 5 papers, Biomedicine 3 papers, Biosciences 2 papers, Biotechnology 1 paper, Botany 2 papers, Chemistry 3 papers, Pharmacy 4 papers, Geoscience 1 paper, Medicine 8 papers, Natural Science 17 papers. Based on the various categories of journal publishers, researchers have diverse knowledge, so it is interesting to consider the research team consisting of researchers with mutually supportive knowledge, for example, informatics, statistics, chemistry, biology, medicine, and pharmacy sciences will contribute positively to each other in a combined research combination Bioinformatics, In Vitro, and In Vivo.

Typhonium flagelliforme plants have low genetics, making them difficult to be cultivated, so researchers carry out special treatments. Some studies carry out the irradiation process on these plants, some studies grow these plants in liquid media and based on the results of their research they are declared successful in growing Typhonium Flagelliforme plants. The irradiation process is a chemical process through irradiation that can allow the original DNA structure to change while moving the planting process from solid media to liquid media is a natural process that allows the DNA structure of the plant to be maintained.

Conclusion

Journal publishers are very diverse, this is because researchers have different knowledge so that *Typhonium flagelliforme* Research as a Cancer Prevention Plant can involve many sciences, so it will be more appropriate to become multi-disciplinary research such as informatics, statistics, chemistry, biology, medicine, and pharmacy. So that the combination of research with Bioinformatics, In Vitro and In Vivo methods can be realized and get more accurate research results.

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