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Author(s): Muhammad Nurul Amin, Budi Yuwono, Natasha Christy Sudarmaji

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Author(s): Vijaya Bharathi. S, Dhanush Kumar S

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Author(s): Sai Sindhu. Ponnathota, Chandra Sekhar Naik. D, M. Janarthan

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Author(s): Abhipsa Anjeela, Subhasmita Subhashree, Birendra Kumar Bindhani, Uday Chand Basak

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Author(s): Hafid Syahputra, Masfria, Nurul Fadila, Yulyana Lamtiurma Siringoringo

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Author(s): Cut Soraya, Sri Rezeki, Liza Meutia Sari, Basri A. Gani, Subhaini Jakfar

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Views: 0 (pdf), 1043 (html)

Access:  Closed Access

Cite: Ch. Bhavani, V. Padmabhushana Chary, P.Mahitha, R. Mahesh, R. Chenchulaxmi, M. Chinnaeswaraiah. Development of a UV Spectrophotometric Method and Validation of Paroxetine Hydrochloride. *Research Journal of Pharmacy and Technology*. 2025;18(10):4716-0. doi: 10.52711/0974-360X.2025.00678 (<https://www.doi.org/10.52711/0974-360X.2025.00678>)

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(AbstractView.aspx?

PID=2025-18-

10-17)

Synthesis of Novel 2-amino-7-chloro-6-fluoro-4-oxo-1,4-dihydroquinoline-3-carbonitrile derivatives and their evaluation for anti-mycobacterial activity (AbstractView.aspx?PID=2025-18-10-18)

Author(s): Beenkumar Prajapati, Haribhai Rabari, Divyeshkumar Doshi, Radadiya Kalpeshkumar

DOI: 10.52711/0974-360X.2025.00679 (<https://www.doi.org/10.52711/0974-360X.2025.00679>)

Views: 0 (pdf), 729 (html)

Access:  Closed Access

Cite: Beenkumar Prajapati, Haribhai Rabari, Divyeshkumar Doshi, Radadiya Kalpeshkumar. Synthesis of Novel 2-amino-7-chloro-6-fluoro-4-oxo-1,4-dihydroquinoline-3-carbonitrile derivatives and their evaluation for anti-mycobacterial activity. *Research Journal of Pharmacy and Technology*. 2025;18(10):4721-6. doi: 10.52711/0974-360X.2025.00679 (<https://www.doi.org/10.52711/0974-360X.2025.00679>)

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(AbstractView.aspx?

PID=2025-18-

10-18)

Developing a Localized Delivery of Polymer-Based Targeted Nanoparticles Through Paclitaxel-Loaded Transdermal Patches for Breast Cancer Therapy: A Proof-of-Concept (AbstractView.aspx?PID=2025-18-10-19)

Author(s): Rakan Abdullah Alsaqer, Shobhana N, N Raghavendra Naveen, Prasiddhi Naik, Prakash Goudanavar, Nagaraja Sreeharsha, Amal Rasul Al Turaifi, Girish Meravanige, Afzal Haq Asif

DOI: 10.52711/0974-360X.2025.00680 (<https://www.doi.org/10.52711/0974-360X.2025.00680>)

Views: 0 (pdf), 630 (html)

Access:  Closed Access

Cite: Rakan Abdullah Alsaqer, Shobhana N, N Raghavendra Naveen, Prasiddhi Naik, Prakash Goudanavar, Nagaraja Sreeharsha, Amal Rasul Al Turaifi, Girish Meravanige, Afzal Haq Asif. Developing a Localized Delivery of Polymer-Based Targeted Nanoparticles Through Paclitaxel-Loaded Transdermal Patches for Breast Cancer Therapy: A Proof-of-Concept. *Research Journal of Pharmacy and Technology*. 2025;18(10):4727-5. doi: 10.52711/0974-360X.2025.00680 (<https://www.doi.org/10.52711/0974-360X.2025.00680>)

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(AbstractView.aspx?
PID=2025-18-
10-19)

A Novel Eco-Friendly approach using the Concept of Hydrotropy for Analytical Estimation of important Medicinal agents (Beta Blocker) (AbstractView.aspx?PID=2025-18-10-2)

Author(s): Harsh D Adhvaryu, Vandana B Patel, Bhoomi H Adhvaryu, Avani N Doshi

DOI: 10.52711/0974-360X.2025.00663 (<https://www.doi.org/10.52711/0974-360X.2025.00663>)

Views: 0 (pdf), 544 (html)

Access:  Closed Access

Cite: Harsh D Adhvaryu, Vandana B Patel, Bhoomi H Adhvaryu, Avani N Doshi. A Novel Eco-Friendly approach using the Concept of Hydrotropy for Analytical Estimation of important Medicinal agents (Beta Blocker). *Research Journal of Pharmacy and Technology*. 2025;18(10):4615-9. doi: 10.52711/0974-360X.2025.00663 (<https://www.doi.org/10.52711/0974-360X.2025.00663>)

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(AbstractView.aspx?
PID=2025-18-
10-2)

Formulation and In vitro Assessment of Valsartan Immediate Release Tablets (AbstractView.aspx?PID=2025-18-10-20)

Author(s): Alaa Abdulrazzaq AL- Nuaimi, Asmaa Abdelaziz Mohamed, Jinan M. Al-Mousawy

DOI: 10.52711/0974-360X.2025.00681 (<https://www.doi.org/10.52711/0974-360X.2025.00681>)

Views: 0 (pdf), 684 (html)

Access:  Closed Access

Cite: Alaa Abdulrazzaq AL- Nuaimi, Asmaa Abdelaziz Mohamed, Jinan M. Al-Mousawy. Formulation and In vitro Assessment of Valsartan Immediate Release Tablets. *Research Journal of Pharmacy and Technology*. 2025;18(10):4736-2. doi: 10.52711/0974-360X.2025.00681 (<https://www.doi.org/10.52711/0974-360X.2025.00681>)

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(AbstractView.aspx?
PID=2025-18-
10-20)

Phytochemical profile and Biological activities of Aquilaria malaccensis Leaf and Stem Bark Extracts: An In vitro study (AbstractView.aspx?PID=2025-18-10-21)

Author(s): Hendera, Irfan Zamzani, Rahmawati

DOI: 10.52711/0974-360X.2025.00682 (<https://www.doi.org/10.52711/0974-360X.2025.00682>)

Views: 0 (pdf), 855 (html)

Access:  Closed Access

Cite: Hendera, Irfan Zamzani, Rahmawati. Phytochemical profile and Biological activities of Aquilaria malaccensis Leaf and Stem Bark Extracts: An In vitro study. *Research Journal of Pharmacy and Technology*. 2025;18(10):4743-1. doi: 10.52711/0974-360X.2025.00682 (<https://www.doi.org/10.52711/0974-360X.2025.00682>)

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(AbstractView.aspx?
PID=2025-18-
10-21)

Assessment of Pharmacological Potency of *Clitoria ternatea* as a Medicinal Herb for In vivo CNS Activity Evaluation (AbstractView.aspx?PID=2025-18-10-22)

Author(s): S. Gejalakshmi, N. Harikrishnan

DOI: 10.52711/0974-360X.2025.00683 (<https://www.doi.org/10.52711/0974-360X.2025.00683>)

Views: 0 (pdf), 692 (html)

Access:  Closed Access

Cite: S. Gejalakshmi, N. Harikrishnan. Assessment of Pharmacological Potency of *Clitoria ternatea* as a Medicinal Herb for In vivo CNS Activity Evaluation. *Assessment of Pharmacological Potency of Clitoria ternatea as a Medicinal Herb for In vivo CNS Activity Evaluation. Research Journal of Pharmacy and Technology.* 2025;18(10):4752-8. doi: 10.52711/0974-360X.2025.00683 (<https://www.doi.org/10.52711/0974-360X.2025.00683>)

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(AbstractView.aspx?

PID=2025-18-
10-22)

Stability Indicating RP-HPLC Method for Estimation of Voxelotor for the Treatment of Sick Cell Disease (AbstractView.aspx?PID=2025-18-10-23)

Author(s): Amitkumar J. Vyas, Drashti J. Gajjar, Saurabh S. Ray, Ajay I. Patel, Ashvin V. Dudhrejiya, Devang B. Sheth, Ashok B. Patel, Sunny R. Shah

DOI: 10.52711/0974-360X.2025.00684 (<https://www.doi.org/10.52711/0974-360X.2025.00684>)

Views: 0 (pdf), 787 (html)

Access:  Closed Access

Cite: Amitkumar J. Vyas, Drashti J. Gajjar, Saurabh S. Ray, Ajay I. Patel, Ashvin V. Dudhrejiya, Devang B. Sheth, Ashok B. Patel, Sunny R. Shah. Stability Indicating RP-HPLC Method for Estimation of Voxelotor for the Treatment of Sick Cell Disease. *Research Journal of Pharmacy and Technology.* 2025;18(10):4759-4. doi: 10.52711/0974-360X.2025.00684 (<https://www.doi.org/10.52711/0974-360X.2025.00684>)

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(AbstractView.aspx?

PID=2025-18-
10-23)

Analytical Method Development and Validation of Ivabradine Hydrochloride using Advanced Analytical Techniques (AbstractView.aspx?PID=2025-18-10-24)

Author(s): Swapnali Suresh Zurange, Subodh Anil Gangurde

DOI: 10.52711/0974-360X.2025.00685 (<https://www.doi.org/10.52711/0974-360X.2025.00685>)

Views: 0 (pdf), 680 (html)

Access:  Closed Access

Cite: Swapnali Suresh Zurange, Subodh Anil Gangurde. Analytical Method Development and Validation of Ivabradine Hydrochloride using Advanced Analytical Techniques. *Research Journal of Pharmacy and Technology*. 2025;18(10):4765-8. doi: 10.52711/0974-360X.2025.00685 (<https://www.doi.org/10.52711/0974-360X.2025.00685>)

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(AbstractView.aspx?
PID=2025-18-
10-24)

The Diagnosis of a Twist: A Rare Obstetric Finding (AbstractView.aspx?PID=2025-18-10-25)

Author(s): Myat San Yi, Khin Than Yee, Amnor Aidiliana Amir, Soe Lwin, Tin Moe Nwe, Ei Mon Mon Kyaw, Mi Mi Khaing, Mon Mon Yee

DOI: 10.52711/0974-360X.2025.00686 (<https://www.doi.org/10.52711/0974-360X.2025.00686>)

Views: 0 (pdf), 564 (html)

Access:  Closed Access

Cite: Myat San Yi, Khin Than Yee, Amnor Aidiliana Amir, Soe Lwin, Tin Moe Nwe, Ei Mon Mon Kyaw, Mi Mi Khaing, Mon Mon Yee. The Diagnosis of a Twist: A Rare Obstetric Finding. *Research Journal of Pharmacy and Technology*. 2025;18(10):4769-2. doi: 10.52711/0974-360X.2025.00686 (<https://www.doi.org/10.52711/0974-360X.2025.00686>)

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(AbstractView.aspx?
PID=2025-18-
10-25)

Computational Screening of *Platostoma palustre* Metabolites for Anti-Inflammation Bioactivity in the Chronic Obstructive Pulmonary Disease Gene Dataset (AbstractView.aspx?PID=2025-18-10-26)

Author(s): Sri Nabawiyati Nurul Makiyah, Rahmah, Ahmad Hafidul Ahkam

DOI: 10.52711/0974-360X.2025.00687 (<https://www.doi.org/10.52711/0974-360X.2025.00687>)

Views: 0 (pdf), 515 (html)

Access:  Closed Access

Cite: Sri Nabawiyati Nurul Makiyah, Rahmah, Ahmad Hafidul Ahkam. Computational Screening of *Platostoma palustre* Metabolites for Anti- Inflammation Bioactivity in the Chronic Obstructive Pulmonary Disease Gene Dataset. *Research Journal of Pharmacy and Technology*. 2025;18(10):4773-0. doi: 10.52711/0974-360X.2025.00687 (<https://www.doi.org/10.52711/0974-360X.2025.00687>)

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(AbstractView.aspx?
PID=2025-18-
10-26)

Molecular Characterization of Protease Enzyme and its Optimization Study (AbstractView.aspx?PID=2025-18-10-27)

Author(s): B Bavishya, Seemone Khadri, C K Ashiga, Bhavaneshwari, Nair Sreecha Chandran

DOI: 10.52711/0974-360X.2025.00688 (<https://www.doi.org/10.52711/0974-360X.2025.00688>)

Views: 0 (pdf), 694 (html)

Access:  Closed Access

Cite: B Bavishya, Seemone Khadri, C K Ashiga, Bhavaneshwari, Nair Sreecha Chandran. Molecular Characterization of Protease Enzyme and its Optimization Study. *Research Journal of Pharmacy and Technology*. 2025;18(10):4781-4. doi: 10.52711/0974-360X.2025.00688 (<https://www.doi.org/10.52711/0974-360X.2025.00688>)

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(AbstractView.aspx?
PID=2025-18-
10-27)

Assessment of Physico-chemical Consumable Water Quality in Tehsil Nadaun, District Hamirpur (Himachal Pradesh), India (AbstractView.aspx?PID=2025-18-10-28)

Author(s): Poonam Talwan, Darsh Gautam, Gaurav Joshi, Sanjay Kumar, Ranjit Singh

DOI: 10.52711/0974-360X.2025.00689 (<https://www.doi.org/10.52711/0974-360X.2025.00689>)

Views: 0 (pdf), 588 (html)

Access:  Closed Access

Cite: Poonam Talwan, Darsh Gautam, Gaurav Joshi, Sanjay Kumar, Ranjit Singh. Assessment of Physico-chemical Consumable Water Quality in Tehsil Nadaun, District Hamirpur (Himachal Pradesh), India. *Research Journal of Pharmacy and Technology*. 2025;18(10):4785-9. doi: 10.52711/0974-360X.2025.00689 (<https://www.doi.org/10.52711/0974-360X.2025.00689>)

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(AbstractView.aspx?
PID=2025-18-
10-28)

Bioanalytical Method Development and its Validation by Using RP-HPLC for Determination of Trimetazidine Dihydrochloride in Human Plasma (AbstractView.aspx?PID=2025-18-10-29)

Author(s): Sahebrao S. Boraste, Deelip V. Derle

DOI: 10.52711/0974-360X.2025.00690 (<https://www.doi.org/10.52711/0974-360X.2025.00690>)

Views: 0 (pdf), 640 (html)

Access:  Closed Access

Cite: Sahebrao S. Boraste, Deelip V. Derle. Bioanalytical Method Development and its Validation by Using RP-HPLC for Determination of Trimetazidine Dihydrochloride in Human Plasma. *Research Journal of Pharmacy and Technology*. 2025;18(10):4790-4. doi: 10.52711/0974-360X.2025.00690 (<https://www.doi.org/10.52711/0974-360X.2025.00690>)

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(AbstractView.aspx?
PID=2025-18-
10-29)

The Effect of Euphorbia milii and Propolis (EMP) Tea on the mRNA of NF-kB Level and the Number of Foam Cells in The Aorta of High Fat Diet Rats (AbstractView.aspx?PID=2025-18-10-3)

Author(s): Ni Made Linawati, Luh Putu Ratna Sundari, I Gusti Kamasan Nyoman Arijana, I Wayan Rai Widarta, I Nyoman Wande, I Wayan Sugiritama, Ni Luh Gede Yoni Komalasari

DOI: 10.52711/0974-360X.2025.00664 (<https://www.doi.org/10.52711/0974-360X.2025.00664>)

Views: 0 (pdf), 612 (html)

Access:  Closed Access

Cite: Ni Made Linawati, Luh Putu Ratna Sundari, I Gusti Kamasan Nyoman Arijana, I Wayan Rai Widarta, I Nyoman Wande, I Wayan Sugiritama, Ni Luh Gede Yoni Komalasari. The Effect of Euphorbia milii and Propolis (EMP) Tea on the mRNA of NF-kB Level and the Number of Foam Cells in The Aorta of High Fat Diet Rats. *Research Journal of Pharmacy and Technology*. 2025;18(10):4620-4. doi: 10.52711/0974-360X.2025.00664 (<https://www.doi.org/10.52711/0974-360X.2025.00664>)

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(AbstractView.aspx?
PID=2025-18-
10-3)

The effect of Pharmacist-led Education and Metabolic Syndrome Screening (EMESYS) on the Clinical Outcome, Adherence, and Quality of Life in Patient with Schizophrenia (AbstractView.aspx?PID=2025-18-10-30)

Author(s): Julaeha Julaeha, Umi Athiyah, Andi Hermansyah

DOI: 10.52711/0974-360X.2025.00691 (<https://www.doi.org/10.52711/0974-360X.2025.00691>)

Views: 0 (pdf), 756 (html)

Access:  Closed Access

Cite: Julaeha Julaeha, Umi Athiyah, Andi Hermansyah. The effect of Pharmacist-led Education and Metabolic Syndrome Screening (EMESYS) on the Clinical Outcome, Adherence, and Quality of Life in Patient with Schizophrenia. *Research Journal of Pharmacy and Technology*. 2025;18(10):4795-2. doi: 10.52711/0974-360X.2025.00691 (<https://www.doi.org/10.52711/0974-360X.2025.00691>)

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(AbstractView.aspx?
PID=2025-18-
10-30)

Phytochemical analysis, antioxidant potential and Identification of Bioactive compounds using GC-MS of the leaf extracts of Clitoria ternatea (AbstractView.aspx?PID=2025-18-10-31)

Author(s): Beaulah Angel P, Manjula K R, Shubha

DOI: 10.52711/0974-360X.2025.00692 (<https://www.doi.org/10.52711/0974-360X.2025.00692>)

Views: 0 (pdf), 1134 (html)

Access:  Closed Access

Cite: Beaulah Angel P, Manjula K R, Shubha. *Phytochemical analysis, antioxidant potential and Identification of Bioactive compounds using GC-MS of the leaf extracts of Clitoria ternatea. Research Journal of Pharmacy and Technology.* 2025;18(10):4803-9. doi: 10.52711/0974-360X.2025.00692 (<https://www.doi.org/10.52711/0974-360X.2025.00692>)

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(AbstractView.aspx?
PID=2025-18-
10-31)

The study of Technological Parameters and Numerical Indicators of the Quality of Raw Materials Inula helenium L. (AbstractView.aspx?PID=2025-18-10-32)

Author(s): Aigul Medeshova, Perizat Orazbayeva, Akniet Dosai, Aizhan Essedova, Karlygash Kaiyrbekova, Zauresh Mukhametzhanova, Aida Shahabayeva, Bekzhan Orazbayev

DOI: 10.52711/0974-360X.2025.00693 (<https://www.doi.org/10.52711/0974-360X.2025.00693>)

Views: 0 (pdf), 935 (html)

Access:  Closed Access

Cite: Aigul Medeshova, Perizat Orazbayeva, Akniet Dosai, Aizhan Essedova, Karlygash Kaiyrbekova, Zauresh Mukhametzhanova, Aida Shahabayeva, Bekzhan Orazbayev. *Research Journal of Pharmacy and Technology.* 2025;18(10):4810-4. doi: 10.52711/0974-360X.2025.00693 (<https://www.doi.org/10.52711/0974-360X.2025.00693>)

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(AbstractView.aspx?
PID=2025-18-
10-32)

Expression of Human Epidermal Receptor 2 (HER-2) and Ki-67 is not associated with the histopathological grade in breast cancer at Abdoel Wahab Sjahranie Hospital, Samarinda, East Borneo, Indonesia (AbstractView.aspx?PID=2025-18-10-33)

Author(s): Nurul Hasanah, Eva Rachmi, Hadi Irawiraman

DOI: 10.52711/0974-360X.2025.00694 (<https://www.doi.org/10.52711/0974-360X.2025.00694>)

Views: 0 (pdf), 568 (html)

Access:  Closed Access

Cite: Nurul Hasanah, Eva Rachmi, Hadi Irawiraman. Expression of Human Epidermal Receptor 2 (HER-2) and Ki-67 is not associated with the histopathological grade in breast cancer at Abdoel Wahab Sjahranie Hospital, Samarinda, East Borneo, Indonesia. *Research Journal of Pharmacy and Technology*. 2025;18(10):4815-0. doi: 10.52711/0974-360X.2025.00694 (<https://www.doi.org/10.52711/0974-360X.2025.00694>)

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(AbstractView.aspx?
PID=2025-18-
10-33)

Sustainable-green synthesis and antimicrobial screening of substituted 4,5-dihydropyrazole derivatives with computational docking insights (AbstractView.aspx?PID=2025-18-10-34)

Author(s): Deepali Wanode, Deweshri Nandurkar, Kumud Bhendarkar, Tahmina Khan, Pramod Khedekar

DOI: 10.52711/0974-360X.2025.00695 (<https://www.doi.org/10.52711/0974-360X.2025.00695>)

Views: 0 (pdf), 545 (html)

Access:  Closed Access

Cite: Deepali Wanode, Deweshri Nandurkar, Kumud Bhendarkar, Tahmina Khan, Pramod Khedekar. Sustainable-green synthesis and antimicrobial screening of substituted 4,5-dihydropyrazole derivatives with computational docking insights. *Research Journal of Pharmacy and Technology*. 2025;18(10):4821-7. doi: 10.52711/0974-360X.2025.00695 (<https://www.doi.org/10.52711/0974-360X.2025.00695>)

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(AbstractView.aspx?
PID=2025-18-
10-34)

Comparative Histochemical Analysis of the Aerial Parts of *Fragaria viridis* and *Fragaria vesca* (Rosaceae) Growing in the Central Kazakhstan Region (AbstractView.aspx?PID=2025-18-10-35)

Author(s): Kurmantayeva G.K., Ishmuratova M.Yu., Atazhanova G.A., Samorodov A.V., Smagulov M.K., Ramazanov A

DOI: 10.52711/0974-360X.2025.00696 (<https://www.doi.org/10.52711/0974-360X.2025.00696>)

Views: 0 (pdf), 534 (html)

Access:  Closed Access

Cite: Kurmantayeva G.K., Ishmuratova M.Yu., Atazhanova G.A., Samorodov A.V., Smagulov M.K., Ramazanov A. Comparative Histochemical Analysis of the Aerial Parts of *Fragaria viridis* and *Fragaria vesca* (Rosaceae) Growing in the Central Kazakhstan Region. *Research Journal of Pharmacy and Technology*. 2025;18(10):4828-2. doi: 10.52711/0974-360X.2025.00696 (<https://www.doi.org/10.52711/0974-360X.2025.00696>)

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(AbstractView.aspx?
PID=2025-18-
10-35)

Formulation and Evaluation of Anti-Protozoal Drug for Emulgel Using New Polymer (AbstractView.aspx?PID=2025-18-10-36)

Author(s): Krishna vagela, Anar Patel, Deshpande Padmanabh Bhagwan, Apexa Shah, Rahul L. Shirole, Sanjesh Rathi, Shubham Singh

DOI: 10.52711/0974-360X.2025.00697 (<https://www.doi.org/10.52711/0974-360X.2025.00697>)

Views: 0 (pdf), 787 (html)

Access:  Closed Access

Cite: Krishna vagela, Anar Patel, Deshpande Padmanabh Bhagwan, Apexa Shah, Rahul L. Shirole, Sanjesh Rathi, Shubham Singh. Formulation and Evaluation of Anti-Protozoal Drug for Emulgel Using New Polymer. *Research Journal of Pharmacy and Technology*. 2025;18(10):4833-8. doi: 10.52711/0974-360X.2025.00697 (<https://www.doi.org/10.52711/0974-360X.2025.00697>)

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(AbstractView.aspx?
PID=2025-18-
10-36)

Formulation Development, Optimization and In vitro Characterization of Ursolic Acid and Boswellic Acid Based Nanoemulsion Drug Delivery System (AbstractView.aspx?PID=2025-18-10-37)

Author(s): Ankur Kapil, Abhishek Pandey, Arnima Sharma, Khushbu Chandel

DOI: 10.52711/0974-360X.2025.00698 (<https://www.doi.org/10.52711/0974-360X.2025.00698>)

Views: 0 (pdf), 885 (html)

Access:  Closed Access

Cite: Ankur Kapil, Abhishek Pandey, Arnima Sharma, Khushbu Chandel. Formulation Development, Optimization and In vitro Characterization of Ursolic Acid and Boswellic Acid Based Nanoemulsion Drug Delivery System. *Research Journal of Pharmacy and Technology*. 2025;18(10):4839-8. doi: 10.52711/0974-360X.2025.00698 (<https://www.doi.org/10.52711/0974-360X.2025.00698>)

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(AbstractView.aspx?
PID=2025-18-
10-37)

Citrulline and Arginine Quantification in Watermelon Rind and Anti-Inflammatory Potential Using In Silico Analysis (AbstractView.aspx?PID=2025-18-10-38)

Author(s): Mukti Priastomo, Amirah Adlia, Rohayati, Valentina Lumbantobing, Wahyu Widayat, Samsul Bahri, I Ketut Adnyana

DOI: 10.52711/0974-360X.2025.00699 (<https://www.doi.org/10.52711/0974-360X.2025.00699>)

Views: 0 (pdf), 1207 (html)

Access:  Closed Access

Cite: Mukti Priastomo, Amirah Adlia, Rohayati, Valentina Lumbantobing, Wahyu Widayat, Samsul Bahri, I Ketut Adnyana. Citrulline and Arginine Quantification in Watermelon Rind and Anti-Inflammatory Potential Using In Silico Analysis. *Research Journal of Pharmacy and Technology*. 2025;18(10):4849-6. doi: 10.52711/0974-360X.2025.00699 (<https://www.doi.org/10.52711/0974-360X.2025.00699>)

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(AbstractView.aspx?
PID=2025-18-
10-38)

Microbial Synthesis of Melanin by *Bacillus proteolyticus* MITWPUME1: Isolation, Characterization, and Potential Application (AbstractView.aspx?PID=2025-18-10-39)

Author(s): Viraj Vivek Gaonkar, Sonam Shrirang Shinde, Humaira Mushtaq Mukadam, Firdaus Alimuddin Sayyed, Kunal Sanjay Sasane, Shikha Vikrant Gaikwad

DOI: 10.52711/0974-360X.2025.00700 (<https://www.doi.org/10.52711/0974-360X.2025.00700>)

Views: 0 (pdf), 997 (html)

Access:  Closed Access

Cite: Viraj Vivek Gaonkar, Sonam Shrirang Shinde, Humaira Mushtaq Mukadam, Firdaus Alimuddin Sayyed, Kunal Sanjay Sasane, Shikha Vikrant Gaikwad. Microbial Synthesis of Melanin by *Bacillus proteolyticus* MITWPUME1: Isolation, Characterization, and Potential Application. *Research Journal of Pharmacy and Technology*. 2025;18(10):4857-4. doi: 10.52711/0974-360X.2025.00700 (<https://www.doi.org/10.52711/0974-360X.2025.00700>)

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(AbstractView.aspx?
PID=2025-18-
10-39)

Improvement of Mechanisms for Increasing the Competitiveness of Pharmaceutical Industries (AbstractView.aspx?PID=2025-18-10-4)

Author(s): Almira Almurzayeva, Kairat Zhakipbekov, Ubaidilla Datkhayev, Olga Posilkina, Akdidar Egizbayeva

DOI: 10.52711/0974-360X.2025.00665 (<https://www.doi.org/10.52711/0974-360X.2025.00665>)

Views: 0 (pdf), 614 (html)

Access:  Closed Access

Cite: Almira Almurzayeva, Kairat Zhakipbekov, Ubaidilla Datkhayev, Olga Posilkina, Akdidar Egizbayeva. Improvement of Mechanisms for Increasing the Competitiveness of Pharmaceutical Industries. *Research Journal of Pharmacy and Technology*. 2025;18(10):4625-4. doi: 10.52711/0974-360X.2025.00665 (<https://www.doi.org/10.52711/0974-360X.2025.00665>)

Read More »

(AbstractView.aspx?
PID=2025-18-
10-4)

Synergistic Cytotoxic effects of Garcinia cowa Leaf Extract and Doxorubicin on MCF-7 Breast Cancer Cells: A Promising Strategy for Enhanced Chemotherapy Efficacy (AbstractView.aspx?PID=2025-18-10-40)

Author(s): Ifora Ifora, Sri Oktavia

DOI: 10.52711/0974-360X.2025.00701 (<https://www.doi.org/10.52711/0974-360X.2025.00701>)

Views: 0 (pdf), 770 (html)

Access:  Closed Access

Cite: Ifora Ifora, Sri Oktavia. Synergistic Cytotoxic effects of Garcinia cowa Leaf Extract and Doxorubicin on MCF-7 Breast Cancer Cells: A Promising Strategy for Enhanced Chemotherapy Efficacy. *Research Journal of Pharmacy and Technology*. 2025;18(10):4865-0. doi: 10.52711/0974-360X.2025.00701 (<https://www.doi.org/10.52711/0974-360X.2025.00701>)

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(AbstractView.aspx?

PID=2025-18-

10-40)

Qualitative and Quantitative Characterization of Curcuminoids Extracted from Curcuma longa cultivated in Mizoram, India (AbstractView.aspx?PID=2025-18-10-41)

Author(s): Laldinchhana, Zonuntluangi, Probin Kr Roy, Renaldy Donlang Nongbet, Lakpa Rinzing Sherpa, Lalzikpuii

DOI: 10.52711/0974-360X.2025.00702 (<https://www.doi.org/10.52711/0974-360X.2025.00702>)

Views: 0 (pdf), 768 (html)

Access:  Closed Access

Cite: Laldinchhana, Zonuntluangi, Probin Kr Roy, Renaldy Donlang Nongbet, Lakpa Rinzing Sherpa, Lalzikpuii. Qualitative and Quantitative Characterization of Curcuminoids Extracted from Curcuma longa cultivated in Mizoram, India. *Research Journal of Pharmacy and Technology*. 2025;18(10):4871-6. doi: 10.52711/0974-360X.2025.00702 (<https://www.doi.org/10.52711/0974-360X.2025.00702>)

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(AbstractView.aspx?

PID=2025-18-

10-41)

Study on Biological Activities of Alloxan Derived Schiff Base Ligand (AbstractView.aspx?PID=2025-18-10-42)

Author(s): Padma Priya Gopalakrishnan, Girija Chamarahalli Ramakrishna Iyer

DOI: 10.52711/0974-360X.2025.00703 (<https://www.doi.org/10.52711/0974-360X.2025.00703>)

Views: 0 (pdf), 442 (html)

Access:  Closed Access

Cite: Padma Priya Gopalakrishnan, Girija Chamarahalli Ramakrishna Iyer. Study on Biological Activities of Alloxan Derived Schiff Base Ligand. *Research Journal of Pharmacy and Technology*. 2025;18(10):4877-1. doi: 10.52711/0974-360X.2025.00703 (<https://www.doi.org/10.52711/0974-360X.2025.00703>)

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(AbstractView.aspx?
PID=2025-18-
10-42)

Histometric Analysis to Perform Purkinje cell Abnormalities in Rats Due to Low doses of Kretek Smoke Exposure (AbstractView.aspx?PID=2025-18-10-43)

Author(s): David Tjahyadi, Edy Parwanto, Hosea Jaya Edy, Joey Joshua Vidova Tjahyadi, Laurentia Gabrielle, Ashaolu Victoria Oladimeji, Seçil Karahüseyin

DOI: 10.52711/0974-360X.2025.00704 (<https://www.doi.org/10.52711/0974-360X.2025.00704>)

Views: 0 (pdf), 584 (html)

Access:  Closed Access

Cite: David Tjahyadi, Edy Parwanto, Hosea Jaya Edy, Joey Joshua Vidova Tjahyadi, Laurentia Gabrielle, Ashaolu Victoria Oladimeji, Seçil Karahüseyin. Histometric Analysis to Perform Purkinje cell Abnormalities in Rats Due to Low doses of Kretek Smoke Exposure. *Research Journal of Pharmacy and Technology*. 2025;18(10):4882-0. doi: 10.52711/0974-360X.2025.00704 (<https://www.doi.org/10.52711/0974-360X.2025.00704>)

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(AbstractView.aspx?
PID=2025-18-
10-43)

GC-MS Analysis of Bioactive Materials in *Amaranthus caudatus* Based on Chemical Polarity (AbstractView.aspx?PID=2025-18-10-44)

Author(s): V. Bhawani, A. Perumal

DOI: 10.52711/0974-360X.2025.00705 (<https://www.doi.org/10.52711/0974-360X.2025.00705>)

Views: 0 (pdf), 861 (html)

Access:  Closed Access

Cite: V. Bhawani, A. Perumal. GC-MS Analysis of Bioactive Materials in *Amaranthus caudatus* Based on Chemical Polarity. *Research Journal of Pharmacy and Technology*. 2025;18(10):4891-6. doi: 10.52711/0974-360X.2025.00705 (<https://www.doi.org/10.52711/0974-360X.2025.00705>)

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(AbstractView.aspx?
PID=2025-18-
10-44)

Evaluation on Antioxidant Properties of Ethanolic Leaves and Branches Extracts of *Nerium indicum* from Jeju Island in Korea (AbstractView.aspx?PID=2025-18-10-45)

Author(s): Min Young Kim

DOI: 10.52711/0974-360X.2025.00706 (<https://www.doi.org/10.52711/0974-360X.2025.00706>)

Views: 0 (pdf), 560 (html)

Access:  Closed Access

Cite: Min Young Kim. Evaluation on Antioxidant Properties of Ethanolic Leaves and Branches Extracts of *Nerium indicum* from Jeju Island in Korea. *Research Journal of Pharmacy and Technology*. 2025;18(10):4897-1. doi: 10.52711/0974-360X.2025.00706 (<https://www.doi.org/10.52711/0974-360X.2025.00706>)

Read More »

(AbstractView.aspx?
PID=2025-18-
10-45)

Sample size calculation, Feasibility, and Safety profile with Olanzapine for preventing Radiation Induced Nausea and Vomiting: Pilot Study for phase III Randomized Placebo-controlled Trial – CTRI No/2022/01/039723 (AbstractView.aspx?PID=2025-18-10-46)

Author(s): Meenu Vijayan, Deb Narayan Dutta, Haridas Nair, Narmadha MP, Sheejamol VS

DOI: 10.52711/0974-360X.2025.00707 (<https://www.doi.org/10.52711/0974-360X.2025.00707>)

Views: 0 (pdf), 705 (html)

Access:  Closed Access

Cite: Meenu Vijayan, Deb Narayan Dutta, Haridas Nair, Narmadha MP, Sheejamol VS. Sample size calculation, Feasibility, and Safety profile with Olanzapine for preventing Radiation Induced Nausea and Vomiting: Pilot Study for phase III Randomized Placebo-controlled Trial – CTRI No/2022/01/039723. *Research Journal of Pharmacy and Technology*. 2025;18(10):4902-8. doi: 10.52711/0974-360X.2025.00707 (<https://www.doi.org/10.52711/0974-360X.2025.00707>)

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(AbstractView.aspx?
PID=2025-18-
10-46)

Curcumin: A Compound in Turmeric That has the Potential to Reduce Tumor Necrosis Factor-Alpha (TNF-a) Levels, and Pain Intensity After High-Intensity Physical Exercise (AbstractView.aspx?PID=2025-18-10-47)

Author(s): Novadri Ayubi, Nining Widyah Kusnanik, Lilik Herawati, Soni Sulistyarto, Anton Komaini, Muhammad Firman Halip, Ainun Zulfikar Rizki, Alvin Afandi, Mohammed Aljunaid, Aulia Putri Srie Wardani, Rais Firlando

DOI: 10.52711/0974-360X.2025.00708 (<https://www.doi.org/10.52711/0974-360X.2025.00708>)

Views: 0 (pdf), 754 (html)

Access:  Closed Access

Cite: Novadri Ayubi, Nining Widyah Kusnanik, Lilik Herawati, Soni Sulistyarto, Anton Komaini, Muhammad Firman Halip, Ainun Zulfikar Rizki, Alvin Afandi, Mohammed Aljunaid, Aulia Putri Srie Wardani, Rais Firlando. Curcumin: A Compound in Turmeric That has the Potential to Reduce Tumor Necrosis Factor-Alpha (TNF-a) Levels, and Pain Intensity After High-Intensity Physical Exercise. *Research Journal of Pharmacy and Technology*. 2025;18(10):4909-4. doi: 10.52711/0974-360X.2025.00708 (<https://www.doi.org/10.52711/0974-360X.2025.00708>)

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(AbstractView.aspx?
PID=2025-18-
10-47)

In-vivo Anti-Ulcer Screening of Methanolic Extract of *Achyranthes aspera* (AbstractView.aspx?PID=2025-18-10-48)

Author(s): *Rahul Vasant Jadhav, Praveen Sharma*

DOI: 10.52711/0974-360X.2025.00709 (<https://www.doi.org/10.52711/0974-360X.2025.00709>)

Views: 0 (pdf), 676 (html)

Access:  Closed Access

Cite: *Rahul Vasant Jadhav, Praveen Sharma. In-vivo Anti-Ulcer Screening of Methanolic Extract of Achyranthes aspera. Research Journal of Pharmacy and Technology. 2025;18(10):4915-0. doi: 10.52711/0974-360X.2025.00709 (<https://www.doi.org/10.52711/0974-360X.2025.00709>)*

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(AbstractView.aspx?
PID=2025-18-
10-48)

Black Tiger Shrimp (*Penaeus monodon*) derived Chitosan Nanoparticle as Cadmium Adsorbent from Fresh Water (AbstractView.aspx?PID=2025-18-10-49)

Author(s): *Annise Proboningrat, Anggun Khoirun Nikmah, Agung Budianto Achmad, Rinza Rahmawati Samsudin, Aswin Rafif Khairullah*

DOI: 10.52711/0974-360X.2025.00710 (<https://www.doi.org/10.52711/0974-360X.2025.00710>)

Views: 0 (pdf), 758 (html)

Access:  Closed Access

Cite: *Annise Proboningrat, Anggun Khoirun Nikmah, Agung Budianto Achmad, Rinza Rahmawati Samsudin, Aswin Rafif Khairullah. Black Tiger Shrimp (Penaeus monodon) derived Chitosan Nanoparticle as Cadmium Adsorbent from Fresh Water. Research Journal of Pharmacy and Technology. 2025;18(10):4821-8. doi: 10.52711/0974-360X.2025.00710 (<https://www.doi.org/10.52711/0974-360X.2025.00710>)*

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(AbstractView.aspx?
PID=2025-18-
10-49)

RNA - Dependent RNA - Polymerase Inhibitor Loaded Mucoadhesive PLGA Nanoparticles: A Study On Formulation and Evaluation of Dry Powder Inhaler (AbstractView.aspx?PID=2025-18-10-5)

Author(s): R. Karthikeyan, V. Vijayan, S. Shanmuganathan, P. Vijayarajkumar, R. Saravanan, S. Brito Raj

DOI: 10.52711/0974-360X.2025.00666 (<https://www.doi.org/10.52711/0974-360X.2025.00666>)

Views: 0 (pdf), 596 (html)

Access:  Closed Access

Cite: R. Karthikeyan, V. Vijayan, S. Shanmuganathan, P. Vijayarajkumar, R. Saravanan, S. Brito Raj. RNA - Dependent RNA - Polymerase Inhibitor Loaded Mucoadhesive PLGA Nanoparticles: A Study On Formulation and Evaluation of Dry Powder Inhaler. *Research Journal of Pharmacy and Technology*. 2025;18(10):4635-0. doi: 10.52711/0974-360X.2025.00666 (<https://www.doi.org/10.52711/0974-360X.2025.00666>)

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(AbstractView.aspx?
PID=2025-18-
10-5)

Telomerase Reverse Transcriptase mRNA as a detection marker in the Plasma of Syrian Breast Cancer patients (AbstractView.aspx?PID=2025-18-10-50)

Author(s): Mubarak R., Soukkarieh Ch., Al-fahoum S.

DOI: 10.52711/0974-360X.2025.00711 (<https://www.doi.org/10.52711/0974-360X.2025.00711>)

Views: 0 (pdf), 517 (html)

Access:  Closed Access

Cite: Mubarak R., Soukkarieh Ch., Al-fahoum S.. Telomerase Reverse Transcriptase mRNA as a detection marker in the Plasma of Syrian Breast Cancer patients. *Research Journal of Pharmacy and Technology*. 2025;18(10):4929-3. doi: 10.52711/0974-360X.2025.00711 (<https://www.doi.org/10.52711/0974-360X.2025.00711>)

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(AbstractView.aspx?
PID=2025-18-
10-50)

The Inhibition of A549 cells from Siam Weeds (*Chromolaena odorata* L.) (AbstractView.aspx?PID=2025-18-10-51)

Author(s): Karlina Amir Tahir, Syatirah Jalaluddin, Muh Fitrah, Ahmad Lalo, Syamsuri Syakri, Upik A. Miskad, Maulita Indrisari, Katsuyoshi Matsunami

DOI: 10.52711/0974-360X.2025.00712 (<https://www.doi.org/10.52711/0974-360X.2025.00712>)

Views: 0 (pdf), 550 (html)

Access:  Closed Access

Cite: Karlina Amir Tahir, Syatirah Jalaluddin, Muh Fitrah, Ahmad Lalo, Syamsuri Syakri, Upik A. Miskad, Maulita Indrisari, Katsuyoshi Matsunami. *The Inhibition of A549 cells from Siam Weeds (*Chromolaena odorata* L.). Research Journal of Pharmacy and Technology. 2025;18(10):4934-8. doi: 10.52711/0974-360X.2025.00712 (<https://www.doi.org/10.52711/0974-360X.2025.00712>)*

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(AbstractView.aspx?

PID=2025-18-

10-51)

Term pregnancy one year after EMA-CO for FIGO stage III gestational choriocarcinoma with pulmonary metastasis and etoposide hypersensitivity: a case report (AbstractView.aspx?PID=2025-18-10-52)

Author(s): Junzhe Zhao, Sonali Prashant Chonkar, Maili Qi, Yash Bhanji Boricha

DOI: 10.52711/0974-360X.2025.00713 (<https://www.doi.org/10.52711/0974-360X.2025.00713>)

Views: 0 (pdf), 540 (html)

Access:  Closed Access

Cite: Junzhe Zhao, Sonali Prashant Chonkar, Maili Qi, Yash Bhanji Boricha. *Term pregnancy one year after EMA-CO for FIGO stage III gestational choriocarcinoma with pulmonary metastasis and etoposide hypersensitivity: a case report. Research Journal of Pharmacy and Technology. 2025;18(10):4939-1. doi: 10.52711/0974-360X.2025.00713 (<https://www.doi.org/10.52711/0974-360X.2025.00713>)*

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(AbstractView.aspx?

PID=2025-18-

10-52)

Compounds Derived from Calamansi Orange Peel Exhibit Potency as HER2 Inhibitors in Breast Cancer (AbstractView.aspx?PID=2025-18-10-53)

Author(s): Audie Joscelino Huang, Windra Prayoga, Yulanda Antonius

DOI: 10.52711/0974-360X.2025.00714 (<https://www.doi.org/10.52711/0974-360X.2025.00714>)

Views: 0 (pdf), 559 (html)

Access:  Closed Access

Cite: Audie Joscelino Huang, Windra Prayoga, Yulanda Antonius. Compounds Derived from Calamansi Orange Peel Exhibit Potency as HER2 Inhibitors in Breast Cancer. *Research Journal of Pharmacy and Technology*. 2025;18(10):4942-8. doi: 10.52711/0974-360X.2025.00714 (<https://www.doi.org/10.52711/0974-360X.2025.00714>)

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(AbstractView.aspx?
PID=2025-18-
10-53)

Red clover (*Trifolium pratense*) Extract Ability Enhances Motor Coordination and Spatial Memory in Parkinson Murine Model (AbstractView.aspx?PID=2025-18-10-54)

Author(s): Haflin Soraya Hutagalung, Aldy Safruddin Rambe, Tri Widyawati, Mustafa Mahmud Amin, Endang Mutiawati Rahayuningsih, Kiking Ritarwan, Puji Pinta Omar Sinurat, Sabri Ibrahim

DOI: 10.52711/0974-360X.2025.00715 (<https://www.doi.org/10.52711/0974-360X.2025.00715>)

Views: 0 (pdf), 590 (html)

Access:  Closed Access

Cite: Haflin Soraya Hutagalung, Aldy Safruddin Rambe, Tri Widyawati, Mustafa Mahmud Amin, Endang Mutiawati Rahayuningsih, Kiking Ritarwan, Puji Pinta Omar Sinurat, Sabri Ibrahim. Red clover (*Trifolium pratense*) Extract Ability Enhances Motor Coordination and Spatial Memory in Parkinson Murine Model. *Research Journal of Pharmacy and Technology*. 2025;18(10):4949-4. doi: 10.52711/0974-360X.2025.00715 (<https://www.doi.org/10.52711/0974-360X.2025.00715>)

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(AbstractView.aspx?
PID=2025-18-
10-54)

Clinical Characteristics of Pediatric Epilepsy Patients Receiving First-Generation Antiseizure Medications Therapy (AbstractView.aspx?PID=2025-18-10-55)

Author(s): *Urfianty, Aidah Juliaty, Idham Jaya Ganda, Jumraini Tammase, Irawan Mangunatmadja, Yanti Leman, Muhammad Yunus Amran, Irfan Idris*

DOI: 10.52711/0974-360X.2025.00716 (<https://www.doi.org/10.52711/0974-360X.2025.00716>)

Views: 0 (pdf), 486 (html)

Access:  Closed Access

Cite: *Urfianty, Aidah Juliaty, Idham Jaya Ganda, Jumraini Tammase, Irawan Mangunatmadja, Yanti Leman, Muhammad Yunus Amran, Irfan Idris. Clinical Characteristics of Pediatric Epilepsy Patients Receiving First-Generation Antiseizure Medications Therapy. Research Journal of Pharmacy and Technology. 2025;18(10):4955-9. doi: 10.52711/0974-360X.2025.00716 (<https://www.doi.org/10.52711/0974-360X.2025.00716>)*

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(AbstractView.aspx?

PID=2025-18-
10-55)

Assessment of Antioxidant and Antibacterial Potential of Leaf Extracts from *Leucaena leucocephala* (AbstractView.aspx?PID=2025-18-10-56)

Author(s): *Dinesh Kumar, Asheesh Kumar Gupta, Prem Saini, Vidhan Chand Bala*

DOI: 10.52711/0974-360X.2025.00717 (<https://www.doi.org/10.52711/0974-360X.2025.00717>)

Views: 0 (pdf), 1092 (html)

Access:  Closed Access

Cite: *Dinesh Kumar, Asheesh Kumar Gupta, Prem Saini, Vidhan Chand Bala. Assessment of Antioxidant and Antibacterial Potential of Leaf Extracts from *Leucaena leucocephala*. Research Journal of Pharmacy and Technology. 2025;18(10):4960-8. doi: 10.52711/0974-360X.2025.00717 (<https://www.doi.org/10.52711/0974-360X.2025.00717>)*

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(AbstractView.aspx?

PID=2025-18-
10-56)

Comparison of Pancreatic Histopathological Features in Wistar Rats Induced with The Diabetogenic Agent Streptozotocin (AbstractView.aspx?PID=2025-18-10-57)

Author(s): Jelita Inayah Sari, Irfan Idris, Suryani As'ad, Husni Cangara

DOI: 10.52711/0974-360X.2025.00718 (<https://www.doi.org/10.52711/0974-360X.2025.00718>)

Views: 0 (pdf), 687 (html)

Access:  Closed Access

Cite: Jelita Inayah Sari, Irfan Idris, Suryani As'ad, Husni Cangara. Comparison of Pancreatic Histopathological Features in Wistar Rats Induced with The Diabetogenic Agent Streptozotocin. *Research Journal of Pharmacy and Technology*. 2025;18(10):4969-6. doi: 10.52711/0974-360X.2025.00718 (<https://www.doi.org/10.52711/0974-360X.2025.00718>)

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(AbstractView.aspx?
PID=2025-18-
10-57)

Microscopic Analysis of the Aerial Parts of *Potentilla bifurca* L. Growing in Central Kazakhstan (AbstractView.aspx?PID=2025-18-10-58)

Author(s): G.T. Murzaliyeva, A.M. Essedova, B.B. Zhakbayeva, O. Zhanat, M.Yu. Ishmuratova

DOI: 10.52711/0974-360X.2025.00719 (<https://www.doi.org/10.52711/0974-360X.2025.00719>)

Views: 0 (pdf), 607 (html)

Access:  Closed Access

Cite: G.T. Murzaliyeva, A.M. Essedova, B.B. Zhakbayeva, O. Zhanat, M.Yu. Ishmuratova. Microscopic Analysis of the Aerial Parts of *Potentilla bifurca* L. Growing in Central Kazakhstan. *Research Journal of Pharmacy and Technology*. 2025;18(10):4977-0. doi: 10.52711/0974-360X.2025.00719 (<https://www.doi.org/10.52711/0974-360X.2025.00719>)

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(AbstractView.aspx?
PID=2025-18-
10-58)

Synthesis, characterization and In-silico study of some 4-nitro-N-(piperidin-4-yl)benzamide derivatives as GPR119 agonists for the treatment of diabetes (AbstractView.aspx?PID=2025-18-10-59)

Author(s): Gourav Jain, Neha Kawathekar

DOI: 10.52711/0974-360X.2025.00720 (<https://www.doi.org/10.52711/0974-360X.2025.00720>)

Views: 0 (pdf), 741 (html)

Access:  Closed Access

Cite: Gourav Jain, Neha Kawathekar. Synthesis, characterization and In-silico study of some 4-nitro-N-(piperidin-4-yl)benzamide derivatives as GPR119 agonists for the treatment of diabetes. *Research Journal of Pharmacy and Technology*. 2025;18(10):4981-9. doi: 10.52711/0974-360X.2025.00720 (<https://www.doi.org/10.52711/0974-360X.2025.00720>)

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(AbstractView.aspx?
PID=2025-18-
10-59)

Evaluation of Antidiabetic potential of a Caper plant species of Gujarat (AbstractView.aspx?PID=2025-18-10-6)

Author(s): Preeti Verma, Khyati Shah, Dharmishtha Parmar, Bhanubhai Suhagia

DOI: 10.52711/0974-360X.2025.00667 (<https://www.doi.org/10.52711/0974-360X.2025.00667>)

Views: 0 (pdf), 547 (html)

Access:  Closed Access

Cite: Preeti Verma, Khyati Shah, Dharmishtha Parmar, Bhanubhai Suhagia. Evaluation of Antidiabetic potential of a Caper plant species of Gujarat. *Research Journal of Pharmacy and Technology*. 2025;18(10):4641-6. doi: 10.52711/0974-360X.2025.00667 (<https://www.doi.org/10.52711/0974-360X.2025.00667>)

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(AbstractView.aspx?
PID=2025-18-
10-6)

Promoting Innovation in The Production of Nutraceuticals: An Examination of Improved Good Manufacturing Practices in Markets That are Regulated or Not (AbstractView.aspx?PID=2025-18-10-60)

Author(s): Bishop Adhikari, D. Nagasamy Venkatesh

DOI: 10.52711/0974-360X.2025.00721 (<https://www.doi.org/10.52711/0974-360X.2025.00721>)

Views: 0 (pdf), 560 (html)

Access:  Closed Access

Cite: Bishop Adhikari, D. Nagasamy Venkatesh. Promoting Innovation in The Production of Nutraceuticals: An Examination of Improved Good Manufacturing Practices in Markets That are Regulated or Not. *Research Journal of Pharmacy and Technology*. 2025;18(10):4990-8. doi: 10.52711/0974-360X.2025.00721 (<https://www.doi.org/10.52711/0974-360X.2025.00721>)

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(AbstractView.aspx?
PID=2025-18-
10-60)

Association between maternal serum C-reactive protein in early pregnancy and spontaneous preterm delivery: a prospective hospital based study in Yangon, Myanmar (AbstractView.aspx?PID=2025-18-10-61)

Author(s): Ei Mon Mon Kyaw, Cherry San

DOI: 10.52711/0974-360X.2025.00722 (<https://www.doi.org/10.52711/0974-360X.2025.00722>)

Views: 0 (pdf), 575 (html)

Access:  Closed Access

Cite: Ei Mon Mon Kyaw, Cherry San. Association between maternal serum C-reactive protein in early pregnancy and spontaneous preterm delivery: a prospective hospital based study in Yangon, Myanmar. *Research Journal of Pharmacy and Technology*. 2025;18(10):4999-2. doi: 10.52711/0974-360X.2025.00722 (<https://www.doi.org/10.52711/0974-360X.2025.00722>)

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(AbstractView.aspx?
PID=2025-18-
10-61)

Development of In Situ Nasal Gel of Moxifloxacin HCl for Brain Targeting: Design, Optimization and In-vitro Evaluation (AbstractView.aspx?PID=2025-18-10-62)

Author(s): Khadija Akhlaque Siddiqui, Prashant Lakshaman Pingale, Sahebrao Sampat Boraste, Sunil Vishvnath Amrutkar, Dattatraya Manohar Shinkar

DOI: 10.52711/0974-360X.2025.00723 (<https://www.doi.org/10.52711/0974-360X.2025.00723>)

Views: 0 (pdf), 505 (html)

Access:  Closed Access

Cite: Khadija Akhlaque Siddiqui, Prashant Lakshaman Pingale, Sahebrao Sampat Boraste, Sunil Vishvnath Amrutkar, Dattatraya Manohar Shinkar. Development of In Situ Nasal Gel of Moxifloxacin HCl for Brain Targeting: Design, Optimization and In-vitro Evaluation. Research Journal of Pharmacy and Technology. 2025;18(10):5003-0. doi: 10.52711/0974-360X.2025.00723 (<https://www.doi.org/10.52711/0974-360X.2025.00723>)

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(AbstractView.aspx?

PID=2025-18-

10-62)

Advanced LC-MS/MS method for the determination of N-Nitroso Atomoxetine in Atomoxetine oral solution: Ensuring drug safety (AbstractView.aspx?PID=2025-18-10-63)

Author(s): Janardhana Swamy Adabala, Hemalatha K., Narendra Angirekula, Mathrusri Annapurna Mukthinuthalapati

DOI: 10.52711/0974-360X.2025.00724 (<https://www.doi.org/10.52711/0974-360X.2025.00724>)

Views: 0 (pdf), 713 (html)

Access:  Closed Access

Cite: Janardhana Swamy Adabala, Hemalatha K., Narendra Angirekula, Mathrusri Annapurna Mukthinuthalapati. Advanced LC-MS/MS method for the determination of N-Nitroso Atomoxetine in Atomoxetine oral solution: Ensuring drug safety. Research Journal of Pharmacy and Technology. 2025;18(10):5011-6. doi: 10.52711/0974-360X.2025.00724 (<https://www.doi.org/10.52711/0974-360X.2025.00724>)

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(AbstractView.aspx?

PID=2025-18-

10-63)

Secondary Metabolites and Antioxidant Activity of Six *Corchorus olitorius* L. Accessions Grown Under Water Deficit Stress Condition. (AbstractView.aspx?PID=2025-18-10-64)

Author(s): S. B. Pholoma, G. Haki, G. Malambane, S. Tshwenyane

DOI: 10.52711/0974-360X.2025.00725 (<https://www.doi.org/10.52711/0974-360X.2025.00725>)

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Cite: S. B. Pholoma, G. Haki, G. Malambane, S. Tshwenyane. Secondary Metabolites and Antioxidant Activity of Six *Corchorus olitorius* L. Accessions Grown Under Water Deficit Stress Condition. *Research Journal of Pharmacy and Technology*. 2025;18(10):5017-6. doi: 10.52711/0974-360X.2025.00725 (<https://www.doi.org/10.52711/0974-360X.2025.00725>)

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Establishing an Insulin-Resistance C2C12 Cell Model: A Systematic Review (AbstractView.aspx?PID=2025-18-10-65)

Author(s): Rita Rakhmawati, Mae Sri Hartati Wahyuningsi, Arko Jatmiko Wicaksono, Mustofa Mustofa, Ahmad Hamim Sadewa

DOI: 10.52711/0974-360X.2025.00726 (<https://www.doi.org/10.52711/0974-360X.2025.00726>)

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A Review on Second Generation (2G) Lactic Acid Production from Lignocellulosic Derived Sugar to Valorize Waste Stream (AbstractView.aspx?PID=2025-18-10-66)

Author(s): Chitra Yadav, Ananthalakshmi Ranganathan, Sarah Iftikhar, Seema Paroha

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Cite: Chitra Yadav, Ananthalakshmi Ranganathan, Sarah Iftikhar, Seema Paroha. A Review on Second Generation (2G) Lactic Acid Production from Lignocellulosic Derived Sugar to Valorize Waste Stream. *Research Journal of Pharmacy and Technology*. 2025;18(10):5035-0. doi: 10.52711/0974-360X.2025.00727 (<https://www.doi.org/10.52711/0974-360X.2025.00727>)

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Review on Nitrosamine: A Potential Genotoxic Impurity (AbstractView.aspx?PID=2025-18-10-67)

Author(s): Baratam Kasinath, Boddu Veeraswami

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A Review on Analytical Methods for Estimation of Abacavir (AbstractView.aspx?PID=2025-18-10-68)

Author(s): Ramgopal M Dhanwad, Pavitra R. Basannavar, Vishakha Saraf

DOI: 10.52711/0974-360X.2025.00729 (<https://www.doi.org/10.52711/0974-360X.2025.00729>)

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Down Regulation of ica A, ica D and mec A genes in Staphylococcus aureus with sub MBC of Allium sativum (AbstractView.aspx?PID=2025-18-10-7)

Author(s): Malathi Vellaiperumal, Bhuvaneshwari Gunasekar, Jayakumar Subramaniam

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Cite: Malathi Vellaiperumal, Bhuvaneshwari Gunasekar, Jayakumar Subramaniam. Down Regulation of ica A, ica D and mec A genes in Staphylococcus aureus with sub MBC of Allium sativum. *Research Journal of Pharmacy and Technology*. 2025;18(10):4647-2. doi: 10.52711/0974-360X.2025.00668 (<https://www.doi.org/10.52711/0974-360X.2025.00668>)

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Ayahuasca: Pharmacological Composition and Potential Benefits (AbstractView.aspx?PID=2025-18-10-70)

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Targeting MAPK Pathways: Novel Therapeutic Approaches for Human Disease (AbstractView.aspx?PID=2025-18-10-71)

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The Role of Pharmacists with Clinical Decision Support Systems in the Drug Related Problems (DRPs) Aspect of Sepsis Patients in the ICU: A Review (AbstractView.aspx?PID=2025-18-10-72)

Author(s): Muh. Irham Bakhtiar, Nanang Munif Yasin, Lucia Rizka Andalusia, Ika Puspita Sari

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Author(s): Kumud P. Bhendarkar, Pramod Khedekar, Deepali M. Wanode, Megha P. Ambatkar

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Nano-engineered biomaterials: An Alternative Route for Drug Delivery in Lung Bioengineering (AbstractView.aspx?PID=2025-18-10-74)

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The Role of Nutrition in Leukemia: A Comprehensive Review of Diet, Supplements and Lifestyle Choices (AbstractView.aspx?PID=2025-18-10-75)

Author(s): Priya Sharma, Archana Kumari, Versha Sharma, Shivali

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Cite: Priya Sharma, Archana Kumari, Versha Sharma, Shivali. The Role of Nutrition in Leukemia: A Comprehensive Review of Diet, Supplements and Lifestyle Choices. *Research Journal of Pharmacy and Technology*. 2025;18(10):5097-0. doi: 10.52711/0974-360X.2025.00736 (<https://www.doi.org/10.52711/0974-360X.2025.00736>)

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Studies of Potential Mung Bean (*Vigna radiata* (L.) Wilczek) Sprouts in Increasing Human Growth Hormone (HGH) and Health benefits in Global Medicine: A Literature Review (AbstractView.aspx?PID=2025-18-10-76)

Author(s): Nurbaety, Jumriani

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Views: 0 (pdf), 1423 (html)

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DOI: 10.52711/0974-360X.2025.00738 (<https://www.doi.org/10.52711/0974-360X.2025.00738>)

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Cite: *Sadia Afrin, Tamanna Sultana, Md. Masud Rana, Md Mizanur Rahman, Akayed Hasan, Ali Mohamod Wasaf Hasan, Mohammad Chand Jamali6, Shafayatun Nahar Tinu, Lama mustafa Al-Tarawneh, Urazbaeva Abdullaevna Dilbar, Nikolaus Syrmos, Md. Rezwan Ahmed Mahedi, Anam Tariq. Ethnomedicinal Significance, Phytochemical Profile, and Therapeutic Potentials of Artocarpus chama (Chapalish): A Review. Research Journal of Pharmacy and Technology. 2025;18(10):5109-8. doi: 10.52711/0974-360X.2025.00738 (<https://www.doi.org/10.52711/0974-360X.2025.00738>)*

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Quality Control Evaluation and In - vitro Equivalence of Various Brands of Marketed Azithromycin Tablets (AbstractView.aspx?PID=2025-18-10-8)

Author(s): *Sadik Almeklafi, Bilal Al-Shahoud, Mohammad Moner, Maya Tarboosh, Reem Ersaly, Baraah Alkazak, Fakhreya Al Hadar*

DOI: 10.52711/0974-360X.2025.00669 (<https://www.doi.org/10.52711/0974-360X.2025.00669>)

Views: 0 (pdf), 674 (html)

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Cite: *Sadik Almeklafi, Bilal Al-Shahoud, Mohammad Moner, Maya Tarboosh, Reem Ersaly, Baraah Alkazak, Fakhreya Al Hadar. Quality Control Evaluation and In - vitro Equivalence of Various Brands of Marketed Azithromycin Tablets. Research Journal of Pharmacy and Technology. 2025;18(10):4653-9. doi: 10.52711/0974-360X.2025.00669 (<https://www.doi.org/10.52711/0974-360X.2025.00669>)*

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Author(s): Darmawansyih, Rosdiana Natzir, Ika Yustisia, Firdaus Hamid, Asri Saleh, Syamsuri Syakri

DOI: 10.52711/0974-360X.2025.00670 (<https://www.doi.org/10.52711/0974-360X.2025.00670>)

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Cite: Darmawansyih, Rosdiana Natzir, Ika Yustisia, Firdaus Hamid, Asri Saleh, Syamsuri Syakri. In silico of Secondary Metabolite Compounds in *Garcinia mangostana* as A Therapy for Type 2 Diabetes. *Research Journal of Pharmacy and Technology*. 2025;18(10):4660-6. doi: 10.52711/0974-360X.2025.00670 (<https://www.doi.org/10.52711/0974-360X.2025.00670>)

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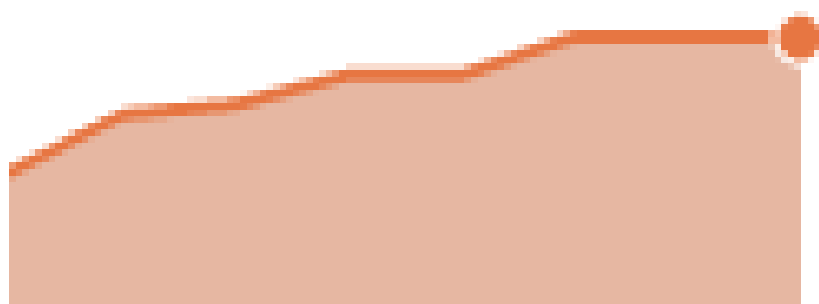
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RESEARCH ARTICLE

Histometric Analysis to Perform Purkinje cell Abnormalities in Rats Due to Low doses of Kretek Smoke Exposure

David Tjahyadi^{1*}, Edy Parwanto², Hosea Jaya Edy³, Joey Joshua Vidova Tjahyadi⁴,
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ABSTRACT:

Facts show that many Indonesians are smokers. Some of these smokers are kretek smokers. Kretek is made from a mixture of tobacco, cloves, and sauce. Kretek smoke is toxic, and affects the cerebellum, especially Purkinje cells. Aim of this study was to determine the effects of kretek smoke on the Purkinje cells of rats. CG (control group) were rats that breathed using normal air (not exposed to kretek smoke). TG (treatment group) were rats that were exposed to smoke of kretek 1 stick/day for 1 month (30 days). Observations were made on the morphology of the rat brain and histology on the cerebellum. Qualitative and quantitative observations were made on Purkinje cells (area, perimeter, length, and width). The nicotine content in the kretek cigarettes used in this study was $3.88 \pm 0.05 \mu\text{g/g}$. Exposure to kretek smoke of 1 stick/day for 1 month in rats demonstrated that the brain did not experience changes in shape, but Purkinje cells in the cerebellum became abnormal in both shape and size. Purkinje cells area of rats in CG was higher than TG ($p = 0.000$). Purkinje cells perimeter of rats in CG was higher than TG ($p = 0.000$). Purkinje cells length of rats in CG was higher than TG ($p = 0.000$). Purkinje cells width of rats in CG was higher than TG ($p = 0.000$). Exposure to kretek smoke of 1 stick/day for 1 month did not change the morphology of the rat brain, but reduced the size of Purkinje cell bodies, and changed the shape from round to tapered as a sign of cell degeneration.

KEYWORDS: Kretek, Low-Dose Kretek Smoke, Nicotine, Cerebellum, Purkinje.

INTRODUCTION:

Indonesia is a group of countries whose population is a smoker in large numbers.¹ Based on the results of the Basic Health Research survey of the Ministry of Health of the Republic of Indonesia in 1918, it shows that 34% of the Indonesian population aged 15+ years are smokers.² Most smokers in Indonesia, namely 73%, smoke kretek.³ The characteristic of kretek is that its composition consists of tobacco, cloves, and sauces.⁴

Cigarette smoke is a toxic mixture. It is known that more than 7000 chemicals are contained in cigarette smoke, more than 4500 as a toxin, and 70 of them are known to be carcinogenic. Nevertheless, there is no doubt that tobacco has been used as an addictive stimulant for

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people around the world.⁵ Moreover, it has been demonstrated that 24 types of kretek cigarettes contained 2.8-33.8mg/stick of eugenol. Fourteen types of 24 types of kretek cigarettes contain 2.8-12.9mg/stick of menthol, 5 of 9 cigarettes contain 3.6-10.8mg/stick.⁶ In addition, that tobacco as the main component of kretek contains nicotine. Nicotine that enters the body when smoking will spread quickly to the brain. Previous studies have shown that nicotine is absorbed systemically after smoking.⁷ Apart from that, the substances contained in cigarette smoke cause addiction.⁸ In this regard, it is stated that the content of this substance influences the development of nerve structures.⁵ Smoking also causes motor damage to the brain.⁹

Our previous study which shown that smoke of filtered kretek decreased the size of bronchioles, but increased the size of respiratory bronchioles. It was further demonstrated that filtered kretek smoke also affected to overexpression of the p53 gene.¹⁰ Moreover, also demonstrated that components of tobacco smoke impact gene expression in *E. coli*.¹¹ Therefore, it is necessary to further investigate the relationship between gene expression manifestations (due to exposure to cigarette smoke) and target cells.

Parts of the brain include the cerebellum. Phylogenetically, the cerebellum is classified into 3 parts, namely paleocerebellum, neocerebellum, and archicerebellum. Based on its anatomical location, the cerebellum is divided as follows: the anterior lobe of the cerebellum, namely the paleocerebellum, the posterior lobe, namely the neocerebellum, and the vestibule of the cerebellum or flocculonodular lobe, namely the archicerebellum. The cerebellum is responsible for motor control. Purkinje cells line up in rows called the Purkinje cell layer. Purkinje cell bodies have unique dendritic branches.¹² The cerebellum can be used as a model for studying the central nervous system. The choice of the cerebellum as a learning model is based on its precise development, so that it can be used as a model for identifying disorders of the central nervous system.¹³

The research results show that in society many people smoke at low doses.^{14,15} Because that, we focused on the effects at low doses of kretek smoke on the rat brain. The effects observed in this study were histological of cells abnormalities in the cerebellum. This focus is a continuation of our previous research.^{16,17}

Although Purkinje cell density has been proven histometrically, it is necessary to know the smoke effect of kretek on brain cell histometrics.¹⁶ So, the purpose of this research is to determine the effect of kretek smoke on changes in "rat Purkinje cells". Changes in "rat Purkinje

cells" both qualitatively and quantitatively can be used as a guideline in a more objective diagnosis of brain tissue disorders.

MATERIAL AND METHODS:

Kretek:

The kretek used in this research were made manually with a composition of tobacco, cloves, and sauce is called as "woor". Tobacco, cloves, and sauce were purchased at the market in the Special Region of Yogyakarta, Indonesia.

Measurement of nicotine levels:

Measurement of nicotine levels in kretek used the CAMAG Linomat 5 "Linomat5_220727" S/N 220727 (1.00.13) instrument. The test method used is Thin Layer Chromatography (TLC) Densitometry. The weight of the sample (kretek) used was 500 mg. Nicotine standards were dissolved in ethanol. Nicotine spot density is read at a wavelength of 265 nm. The retardation factor (Rf) value in measuring nicotine levels is 0.64, with a standard of 1010 ug/mL. The formula used to calculate nicotine levels is as follows:

$$\begin{aligned} \text{Nicotine in the sample (ug)} &= \frac{(\text{sample area} - b)}{a} \\ \text{LoD device (ug)} &= \frac{(1.97 \times b) - b}{a} \\ \text{LoD in sample} &= \frac{\text{LoD device (ug)}}{\text{Number of spottings in the sample (ug)}} \times 1000 \\ \text{Sample nicotine levels (ug/g)} &= \frac{\text{Nicotine levels in the device (ug)}}{\text{Number of samples tested (ug)}} \times 1000 \end{aligned}$$

Screening GC MS:

The GC-MS tool used to measure the substance content in kretek requires first calibrating the tool. The sample (kretek) was added with 1.5 mL of ethanol in a microtube, then vortexed until homogeneous. Next, the solution was centrifuged at 9500 rpm for 5 minutes. The supernatant is put into a gas chromatography vial, then injected into the gas chromatography column. Column used HP-5ms Ultra Inert Columns.

Ethical clearance:

We obtained the ¹ ethical clearance No. 058/KER/FK/IU2024 from the Research Ethics Commission, Faculty of Medicine, Universitas Trisakti, Jakarta, Indonesia.

Animal:

The experimental animals used were the Sprague-Dawley rats. The number of rats is 16, male gender, age: 2 – 3 months, body weight 150 to 200grams, in good health as declared by a veterinarian. During the study, rats were placed in cages individually. Rat cages were placed in an animal treatment room. The room temperature used for these experimental was 24 - 28°C, with a room humidity of 50-60%. The room lighting used

was artificial fluorescence with a light and dark cycle of 12:12 hours. The rats were given food and drink sufficiently (at libitum), based to standards.

Sample size calculated with the minimum sample size formula, namely $N = 10: (2 - 1) + 1 = 5$ rats, while the maximum sample size was $N = 20: (2 - 1) + 1 = 10$ rats.¹⁸ Researchers used 8 rats for each treatment group. Rats were sacrificed after the experiment was completed. Brain organs were taken to make slide preparations.

Treatment:

Acclimatization for 1 week was carried out on all rats included in the study. During acclimatization, rat was in individual cages placed in the animal treatment room. The rats were given food and drink at libitum, according to standards. During acclimatization, rats were not treated. After acclimatization, the rats were randomly grouped into 2 groups, each group consisting of 8 rats. Control group in these studies is CG. CG is rats breathe normal air, not exposed to smoke of kretek. Treatment group in this study is TG, the rats were given treatment, namely exposure to smoke of kretek, with a dose of 1 cigarette/day. The duration of exposure to smoke of kretek on both groups (CG and TG) was 1 month (30 days).

The size of the glass box for treatment is 45 cm long, 35 cm wide and 20cm high (31,500 cm³). The glassbox as a place for cigarette smoke exposure is equipped with a pipe connected to an electric pump. After the kretek is burned, and the electric pump is turned on, the smoke of kretek enters the glass box, then is inhaled by the experimental rats.

Treatment in TG for 10 minutes, every morning for 1 month (30 days). After being treated, the rats were anesthetized to death. We used ketamine (100mg/kg body weight), and xylazine (10mg/kg body weight) intraperitoneally. Animals that had been sacrificed by euthanasia, then their brains were taken, and stored in bottles containing 10% neutral buffered formalin (NBF) solution. The next step is that the brains are used to make histological preparations.

Research diagram:

Research diagram is presented in Figure 1.

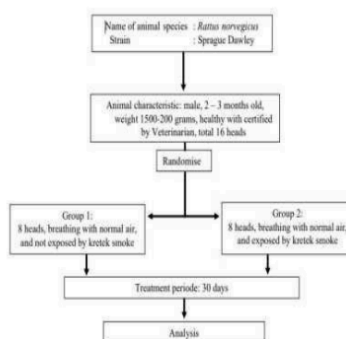


Figure 1. Research flow diagram

Hematoxylin and eosin staining:

NBF 10% is used to fix the brain tissue. Next, the brain tissue was made into slides with hematoxylin and eosin staining as done in previous studies.^{16, 17}

Qualitative observed of Purkinje cells:

Cerebellum slide images were documented using Optilab Advance Plus. Analysis of the slide images used ImageRast¹⁴, Optilab Advance Plus, and Image Raster 3 devices (<https://miconos.ac.id/new/support/download>). Observation of Purkinje cell abnormalities was shown if abnormalities in cell shape were found. The shape of Purkinje cells between the control group and the treatment group was compared qualitatively.

Quantitative measurement of Purkinje cells:

Cerebellum image documentation has been carried out with Optilab Advance Plus. Quantitative measurement of Purkinje cells was carried out with Image Raster 3 (<https://miconos.ac.id/new/support/download>). Cytometry parameters of Purkinje cells are area, perimeter, length, and width. Three researchers were involved in the measurement of Purkinje cell cytometry. Measurement data are displayed as mean and standard deviation (SD). Independent sample t test was used to compare differences in Purkinje cell cytometry between groups. We used $p < 0.05$ for differences between groups.

RESULTS:

Nicotine levels:

Chromatogram obtained using <win CATS Planar Chromatography Manager= and the standard curve used to measure nicotine levels of kretek are presented in Figure 2.

Table 1. Nicotine levels in kretek cigarettes

NS	R	SW (g)	SSV (μ L)	AFS mL	Freq	NDS (μ g)	A	NIS (μ g)	NIDS (μ g/g)	Avr (μ g/g)
1	1	0.5048	2.5	5	1	252.4	5916.1	0.99	3.92	3.92
	2	0.5048	2.5	5	1	252.4	5916.1	0.99	3.92	
2	1	0.5022	2.5	5	1	251.1	5840.5	0.975	3.88	3.84
	2	0.5022	2.5	5	1	251.1	5724.9	0.951	3.79	
3	1	0.5034	2.5	5	1	251.6	5752.6	0.957	3.80	3.80
	2	0.5034	2.5	5	1	251.8	5759.3	0.958	3.81	
4	1	0.5029	2.5	5	1	251.2	5838.4	0.974	3.88	3.88
	2	0.5029	2.5	5	1	251.2	5852.5	0.977	3.89	
5	1	0.5041	2.5	5	1	251.9	5798.4	0.966	3.84	3.91
	2	0.5041	2.5	5	1	251.9	5976.3	1.002	3.98	
6	1	0.5046	2.5	5	1	252.2	5921.2	0.991	3.93	3.93
	2	0.5046	2.5	5	1	252.2	5928.3	0.993	3.94	

Avr $\pm$ SD 3.88 $\pm$ 0.05

Abbreviations: NS = Number of Sample, R = Replicants, SW = Sample weight, SSV = Sample spotting volume, AFS = Add final sample, F = Frequency, NDS = Number of deep spots, A = area, NIS = nicotine in the sample, NIDS = Nicotine levels in dry samples, Avr = average, g = gram, μ L = micro liter, mL = milli liter, μ g = micro gram, μ g/g = micro gram per gram, SD = standard of deviation.

The nicotine content in kretek used in this study was 3.88 $\pm$ 0.05 μ g/g.

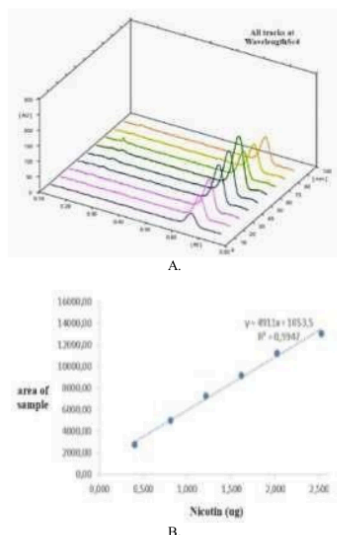


Figure 2. Chromatogram, and Standard curve for nicotine levels. A. 3-D chromatogram obtained using winCATS Planar Chromatography Manager. B = Standard curve for nicotine levels.

Nicotine levels in kretek cigarettes are presented in Table 1.

Content of substances in kretek:

Based on the GC-MS chromatogram, there are 99 substances measured in kretek (all types of substances are not shown in this paper). Substances contained in kretek with high amounts including ethyl-

diisopropylacetamide ($C_{10}H_{21}NO$), Pyridine, 2-(1-methyl-2-pyrrolidinyl)- ($C_{10}H_{14}N_2$), 3-Allyl-6-methoxyphenol ($C_{10}H_{12}O_2$), Caryophyllene ($C_{15}H_{24}$), 10-Octadecenoic acid, methyl ester ($C_{19}H_{36}O_2$), 1-Heptatriacotanol ($C_{37}H_{76}O$).

Brain morphology and histological structure of the cerebellum of Sprague Dawley rats:

Brain morphology and histological structure of the cerebellum of rats is presented in Figure 3.

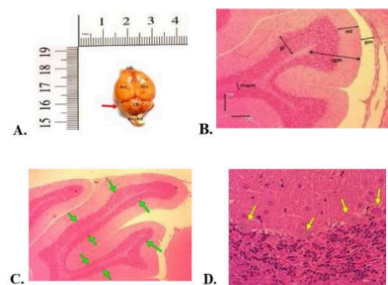


Figure 3. Brain morphology and histological structure of the cerebellum of rats.

A, Sprague Dawley rats9 brain. Cerebellum preparations were made in cross sections indicated by red arrows. B. Histology of the cerebellum of Sprague Dawley rats, hematoxylin and eosin staining, objective 10 x. ob = olfactory bulb, rcc = right cerebral cortex, lcc = left cerebral cortex, cb = cerebellum, mobs = medulla oblongata of brain stem, pm = pia matter, ml = molecular layer, cgm = cortex of grey matter, gl = granular cell layer, mwm = medulla of white matter. C. Purkinje cells at the edge of the granular cell layer (green

18 yellow arrow), hematox 18 and eosin staining, objective 10 x. D. Cell Purkinje (yellow arrow), hematoxylin and eosin staining, objective 40 x.

The brain morphology of Rats looks at the olfactory bulb (ob), left and right cerebral cortex (lcc and rcc), cerebellum (cb), and medulla oblongata of brain stem (mobs). The histological structure of the cerebellum appears in the pia matter (pm), molecular layer (ml), cortex of grey matter (cgm), granular cell layer (gl), medulla of white matter (mwm), Purkinje cells at the edge of the granular cell layer (green yellow arrow). The morphology of the rat's brain between CG was no different compared to TG. Morphologically, the part of the rat's brain between CG was no different compared to TG. All rat brains in this study had the same parts, including ob, lcc, rcc, cb, and mobs.

Qualitative comparison of the cerebellum between treatment groups

Purkinje cells are located at the edge of the granular cell layer of the rat cerebellum in both groups (CG and TG). The appearance of Purkinje cells in CG appears round, while in TG they appear smaller and tapered. Based on this appearance, Purkinje cells in CG appear to have a normal histological structure, while Purkinje cells in TG appear abnormal. A comparison of the appearance of Purkinje cells in rats between groups is presented in Figure 4.

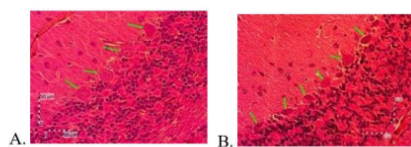


Figure 4. Comparison of the appearance of the Purkinje cells of rats between CG compared to TG. A. Purkinje cells in CG. B. Purkinje cells in TG. Purkinje cells in CG (A) and TG (B) stained with hematoxylin and eosin, and objective 40 x. CG rats breathe using ordinary air without exposure to smoke of kretek. TG, the group of rats exposed to smoke of kretek 1 stick/day for 1 month (30 days) of treatment. Purkinje cells are indicated by green yellow arrows.

Purkinje cell cytometry:

A cytometry comparison (area, perimeter, length, and width) of the Purkinje cells of rats between CG compared to TG are presented in Figure 5.

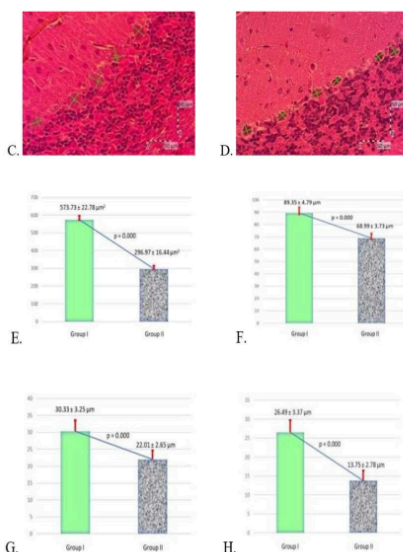
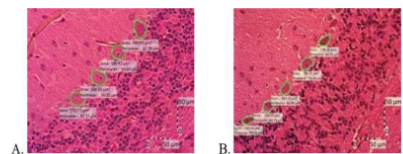


Figure 5. Cytometry comparison of Purkinje cells in rats

A. Area and perimeter of Purkinje cells in CG. B. Area and perimeter of Purkinje cells in TG. C. Length and width of Purkinje cells in CG (control). D. Length and width of Purkinje cells in TG. Purkinje cells in rats were stained with hematoxylin and eosin, 40x objective. E. Area comparison of Purkinje cells between CG compared to TG. F. Perimeter comparison of Purkinje cells between CG compared with TG. G. Length comparison of Purkinje cells between CG compared with TG. H. Width comparison of Purkinje cells between CG compared with TG. CG (control), rats breathe using ordinary air without exposure to kretek smoke. TG, the rat's group that exposed to kretek smoke 1 stick/day for 1 month (30 days) of treatment. Purkinje cells are indicated by green yellow arrows.

Mean value of Purkinje cells area of rats in CG is $573.73 \mu\text{m}^2$, with SD $22.78 \mu\text{m}^2$, number of samples 48, with 95% lower and upper of confidence interval (CI) 567.30 and $579.93 \mu\text{m}^2$, respectively. Mean value of Purkinje cells area of rats in TG is $296.97 \mu\text{m}^2$; with SD $16.44 \mu\text{m}^2$; number of samples 48, with 95% lower and upper of CI 292.46 and $301.79 \mu\text{m}^2$, respectively. Levene's test for equality of variance of Purkinje cells area with F value 4.704; $p = 0.033$; p value of t-test for equality of means 0.000; with $t = 68.26$; $df = 85.51$. Purkinje cells area of rats in CG was higher than TG ($p = 0.000$).

Mean value of Purkinje cells perimeter of rats in CG is 89.35 μm , with SD 4.79 μm , number of samples 48, with 95% lower and upper of CI 87.98 and 90.63 μm , respectively. Mean value of Purkinje cells perimeter of rats in TG is 68.99 μm ; with SD 3.73 μm ; number of samples 48, with 95% lower and upper of CI 67.93 and 70.02 μm , respectively. Levene's test for equality of variances of Purkinje cells area with F value 2.70; $p = 0.104$; p value of t-test for equality of means 0.000, with $t = 23.24$; $df = 94$. Purkinje cells perimeter of rats in CG was higher than TG ($p = 0.000$).

Mean value of Purkinje cells length of rats in CG is 30.33 μm , with SD 3.25 μm , number of samples 48, with 95% lower and upper of CI 29.43 and 31.23 μm , respectively. Mean value of Purkinje cells length of rats in TG is 22.01 μm , with SD 2.65 μm , number of samples 48, 95% lower and upper of CI 21.27 and 22.79 μm , respectively. Levene's test for equality of variances of Purkinje cells area with F value 3.79; $p = 0.054$, p value of t-test for equality of means 0.000, with $t = 13.75$; $df = 94$. Purkinje cells length of rats in CG was higher than TG ($p = 0.000$).

Mean value of Purkinje cells width of rats in CG is 26.49 μm , with SD 3.37 μm , number of samples 48, with 95% lower and upper of CI 25.56 and 27.38 μm , respectively. Mean value of Purkinje cells width of rats in TG is 13.75 μm , with SD 2.78 μm , number of samples 48, with 95% lower and upper of CI 12.95 and 14.56 μm , respectively. Levene's test for equality of variances of Purkinje cells width with F value 1.033, $p = 0.312$, p value of t-test for equality of means 0.000, with $t = 20.21$, $df = 94$. Purkinje cells width of rats in CG was higher than TG ($p = 0.000$).

DISCUSSION:

The nicotine content in kretek used in this study was $3.88 \pm 0.05 \mu\text{g/g}$. It has been shown that tobacco use is associated with nicotine dependence.¹⁹ It has been proven that nicotine causes addiction in users.²⁰ The consequence of a smoker is that the nicotine levels in the body increase. Although there are other alternatives in the form of electronic cigarettes which are intended to reduce nicotine levels.^{21,22,23} However, it is important to note that e-cigarettes can also use nicotine as a vaporizable substance.²⁴ Reducing nicotine levels in kretek needs to be done because it has the potential to provide benefits to public health.^{25,26, 27} Despite the occurrence of hyperexcitability reactions,²⁸ smoking cessation is better for maintaining better health. Therefore, nicotine replacement therapy (NRT) is needed to replace nicotine from cigarettes used by smokers.²⁹ It has been clearly stated that cigarettes cause health problems not only in the respiratory tract but also in body organs up to the molecular level, for example in

antioxidant enzymes.³⁰ Regarding the substance content in kretek, in this study, we did not measure eugenol levels. The results of other studies demonstrate that the eugenol levels in kretek range from 2.8-33.8 mg/stick.⁶

There are several substances in kretek that are contained in high amounts, including Pyridine, Caryophyllene (C₁₅H₂₄), methyl ester (C₁₉H₃₆O₂), and 1-Heptatriacotanol (C₃₇H₇₆O). Apart from that, there are also molecules of ethyl-diisopropylacetamide (C₁₀H₂₁NO), 3-Allyl-6-methoxyphenol (C₁₀H₁₂O₂), 2-(1-methyl-2- pyrrolidinyl)- (C₁₀H₁₄N₂), and 10-Octadecenoic acid. Although we did not check eugenol levels, the kretek used in this study contained caryophyllene. We know that caryophyllene is an essential herbal oil, including clove oil. Caryophyllene has been proven to be anti-inflammatory by inhibiting inflammatory mediators, for example inducible Interleukin 1 beta (IL-1 β) and nitric oxide synthase (iNOS).^{31, 32} Pyridine and its derivatives are heterocyclic compounds with low molecular weight. Even though our research results show high levels in cigarette smoke, pyridine is used as an anti-oxidant and anti-bacterial. Apart from that, pyridine is also used to treat various diseases, for example cardiovascular disease, anti-cancer, and anti-coagulant.³³ Based on the results of previous studies, we suggest that further research be conducted on the relationship between the content of substances in kretek and macrophage recruitment as an inflammatory response due to exposure to cigarette smoke.³⁴

Fatty acid methyl esters (FAME) occur through the transesterification process of fat with methanol. FAME is found for example in biodiesel, usually obtained from vegetable oils through transesterification. Apart from that, FAME is also used to produce detergents and biodiesel.³⁵ Although it has been demonstrated that there is a correlation between fatty acid metabolic pathways and acute lung injury.³⁶ Because the high fatty acid content in kretek is a source of exposure to lung organs, in the future research needs to be focused on the fatty acid aspect of lung injury, as well as other organs. Heptatriacotanol molecules are also contained in kretek. Heptatriacotanol acts as an anti-oxidant, anti-inflammatory, and anti-cancer.³⁷

In this study, Sprague Dawley's brain exposed to kretek smoke with low doses appeared normal, and did not differ morphologically compared to the group that was not exposed (CG as a control group). Exposure to kretek smoke with low doses, namely 1 stick/day for 1 month (30 days), did not affect Sprague Dawley's brain morphology. We compared the brain morphology of rats qualitatively. When compared with the results of previous studies, the morphology of the rat brain in this

study appears to be the same size. Moreover, it is also shown that the cerebellum appears to be the largest part of the rat brain. The olfactory bulb is in the rostral part of the cerebrum, while the caudal part of the cerebrum is the cerebellum, and the ventral part is the brainstem.^{38,39}

Changes in the shape of Purkinje cells in the cerebellum of rats exposed to smoke of kretek 1 stick/day for 1 month (30 days) showed abnormalities. The Purkinje cell abnormalities in this study were like brain abnormalities in rats exposed to tobacco smoke for a long time.¹⁵ Previous research demonstrated that in adult rats exposed to very low doses of tobacco smoke for a long time found a reduction in immature neurons in the brain.⁴⁰ Although our previous research has not measured Purkinje cell cytometry, our study showed that exposure to smoke of cigarette 1 stick/day for 3 months decreased Purkinje cell density (in the cerebellar cortex).¹⁶ These abnormal Purkinje cells are a sign of degeneration. Purkinje cells change size and shape, from large and round to smaller and tapered (Figure 5). The occurrence of pathological conditions of Purkinje cells in this study is in line with the oxidative stress theory. This Purkinje cell condition occurs due to oxidative stress. Oxidative stress can originate both exogenously and endogenously. Cigarette smoke contains chemical compounds that trigger compounds in cells to form proinflammatory compounds. The modulation that occurs in these intracellular proinflammatory pathways results in pathological conditions.⁴¹ This fact is reinforced by research results that demonstrate cigarette smoke causes inflammation with various mechanisms of action.^{42, 43}

The results of this research, which showed a cytometry decrease in Purkinje cells in a TG are in line with the result of previous research. Previous research results that are in accordance with the results of this study include the nicotine content in tobacco. Research results have demonstrated that apart from nicotine, tobacco also contains alkaloids and other secondary metabolites.⁴⁴ In more detail, cigarettes purchased on the market contain about 1.5% alkaloids by weight of tobacco. Tobacco contributes about 95% of the total alkaloid content.⁴⁵ It has been demonstrated that the nicotine in cigarette smoke decreases brain volume. It was further shown that individuals who actively smoke daily were strongly associated with a decrease in total grey matter. In more detail it was demonstrated that increasing the smoking dose had a greater effect on reducing brain volume.⁴⁶ It is not just the smoke effect of kretek on the brain, it has been further demonstrated that smoke of kretek also affects the brain reward threshold. The results of previous research on rats exposed to nicotine at various concentrations per cigarette (0.028; 0.07; 0.13; 0.272; and 0.84 mg/stick) showed that nicotine lowered the brain reward threshold.⁴⁷

Previous research results show that nicotine in tobacco has a serious impact on the body through various multidimensional pathways. Apart from that, nicotine also has an impact on nerve health. The exact mechanism of nicotine's effect on nerve health is not yet known.⁵ The influence of nicotine in cigarette smoke on neurological health is certainly related to the decreased in Purkinje cell cytometry in the results of this study. The reduction in Purkinje cell cytometry in the results of this research is in line with the results of previous studies. The results of previous research demonstrated that smoking decreased grey matter volume (GMV) in most brain areas. The GMV measurement was carried out using voxel-based morphometry (VBM). The results of this study also shown that cigarette smoke reduces GMV in the cerebellum.⁴⁸ Our results are in line with other studies showed that exposure to kretek smoke can impact brain structure and function.⁴⁹ Moreover, it has been shown that low dose cigarette smoke exposure also demonstrated of overexpression of p53 gene.¹⁰

Purkinje cell abnormalities in the group of mice exposed to cigarette smoke need to be compared with the control group, this is important in histopathology. Changes in Purkinje cell size include changes in area, perimeter, length, and width. The appearance of abnormal Purkinje cells is characterized by a smaller size than normal ones, so that the area, perimeter, length, and width are also reduced. Likewise, the tapered appearance of Purkinje cells also shows that the size of the area, perimeter, length, and width decreases. Quantitative changes to Purkinje cells (area, perimeter, length, and width) affect the qualitative appearance of the cells. Based on the cerebellum is a brain region that plays an important role in motor control,¹² then in the future it is necessary to investigate the relationship between Purkinje cell abnormalities and motor function.

LIMITATION:

The limitation of this research is that we did not measure the substance content in kretek smoke, for example levels total alkaloids, tar, and eugenol. These substances certainly affect the cerebellum of mice, especially the occurrence of Purkinje cell abnormalities. We also did not correlate the levels of substances in kretek smoke with the degree of Purkinje cell abnormalities. Apart from that, we also did not measure the thickness of each layer of the cerebellum, the characteristics of the cells in the granule cell layer of the cerebellum. Abnormalities in the size and shape of Purkinje cells which are associated with motor function are important to study because they can be used in diagnosis both at the cellular and tissue levels.^{50,51}

CONCLUSION:

Exposure to low doses of kretek smoke of 1 stick/day for 1 month (30 days) in rats did not affect morphological changes in the brain. Kretek smoke 1 stick/day for 30 days reduces the size of Purkinje cell bodies and changes the shape from round to tapered. In the future, it is necessary to investigate the clinical implications of Purkinje cell abnormalities on motor function due to kretek smoke exposure. More specifically, it is necessary to examine abnormalities in the size and shape of Purkinje cells that experience degeneration due to kretek smoke exposure.

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CONFLICT OF INTERESTS:

All authors declare that there is no conflict of interest.

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ETHICAL STATEMENT:

Ethical approval for this research is Number: 058/KER/FK/IU/2024 by the Research Ethics Commission, Faculty of Medicine, Universitas Trisakti, Jakarta, Indonesia.

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AUTHORS CONTRIBUTIONS:

DT, EP, HJE = Schemed, and designed experiment. DV, HJE, EP, AVO, SK = data collecting, analysis, and the results interpretation. EP, JJNT, LG, HJE = images review, and processing. DV, HJE, EP, SK = preparation of writing a manuscript. All author9s = reviewing and approved the final manuscript.

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RESEARCH ARTICLE

Histometric Analysis to Perform Purkinje cell Abnormalities in Rats Due to Low doses of Kretek Smoke Exposure

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ABSTRACT:

Facts show that many Indonesians are smokers. Some of these smokers are kretek smokers. Kretek is made from a mixture of tobacco, cloves, and sauce. Kretek smoke is toxic, and affects the cerebellum, especially Purkinje cells. Aim of this study was to determine the effects of kretek smoke on the Purkinje cells of rats. CG (control group) were rats that breathed using normal air (not exposed to kretek smoke). TG (treatment group) were rats that were exposed to smoke of kretek 1 stick/day for 1 month (30 days). Observations were made on the morphology of the rat brain and histology on the cerebellum. Qualitative and quantitative observations were made on Purkinje cells (area, perimeter, length, and width). The nicotine content in the kretek cigarettes used in this study was $3.88 \pm 0.05 \mu\text{g/g}$. Exposure to kretek smoke of 1 stick/day for 1 month in rats demonstrated that the brain did not experience changes in shape, but Purkinje cells in the cerebellum became abnormal in both shape and size. Purkinje cells area of rats in CG was higher than TG ($p = 0.000$). Purkinje cells perimeter of rats in CG was higher than TG ($p = 0.000$). Purkinje cells length of rats in CG was higher than TG ($p = 0.000$). Purkinje cells width of rats in CG was higher than TG ($p = 0.000$). Exposure to kretek smoke of 1 stick/day for 1 month did not change the morphology of the rat brain, but reduced the size of Purkinje cell bodies, and changed the shape from round to tapered as a sign of cell degeneration.

KEYWORDS: Kretek, Low-Dose Kretek Smoke, Nicotine, Cerebellum, Purkinje.

INTRODUCTION:

Indonesia is a group of countries whose population is a smoker in large numbers.¹ Based on the results of the Basic Health Research survey of the Ministry of Health of the Republic of Indonesia in 1918, it shows that 34% of the Indonesian population aged 15+ years are smokers.² Most smokers in Indonesia, namely 73%, smoke kretek.³ The characteristic of kretek is that its composition consists of tobacco, cloves, and sauces.⁴

Cigarette smoke is a toxic mixture. It is known that more than 7000 chemicals are contained in cigarette smoke, more than 4500 as a toxin, and 70 of them are known to be carcinogenic. Nevertheless, there is no doubt that tobacco has been used as an addictive stimulant for

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people around the world.⁵ Moreover, it has been demonstrated that 24 types of kretek cigarettes contained 2.8-33.8mg/stick of eugenol. Fourteen types of 24 types of kretek cigarettes contain 2.8-12.9mg/stick of menthol, 5 of 9 cigarettes contain 3.6-10.8mg/stick.⁶ In addition, that tobacco as the main component of kretek contains nicotine. Nicotine that enters the body when smoking will spread quickly to the brain. Previous studies have shown that nicotine is absorbed systemically after smoking.⁷ Apart from that, the substances contained in cigarette smoke cause addiction.⁸ In this regard, it is stated that the content of this substance influences the development of nerve structures.⁵ Smoking also causes motor damage to the brain.⁹

Our previous study which shown that smoke of filtered kretek decreased the size of bronchioles, but increased the size of respiratory bronchioles. It was further demonstrated that filtered kretek smoke also affected to overexpression of the p53 gene.¹⁰ Moreover, also demonstrated that components of tobacco smoke impact gene expression in *E. coli*.¹¹ Therefore, it is necessary to further investigate the relationship between gene expression manifestations (due to exposure to cigarette smoke) and target cells.

Parts of the brain include the cerebellum. Phylogenetically, the cerebellum is classified into 3 parts, namely paleocerebellum, neocerebellum, and archicerebellum. Based on its anatomical location, the cerebellum is divided as follows: the anterior lobe of the cerebellum, namely the paleocerebellum, the posterior lobe, namely the neocerebellum, and the vestibule of the cerebellum or flocculonodular lobe, namely the archicerebellum. The cerebellum is responsible for motor control. Purkinje cells line up in rows called the Purkinje cell layer. Purkinje cell bodies have unique dendritic branches.¹² The cerebellum can be used as a model for studying the central nervous system. The choice of the cerebellum as a learning model is based on its precise development, so that it can be used as a model for identifying disorders of the central nervous system.¹³

The research results show that in society many people smoke at low doses.^{14,15} Because that, we focused on the effects at low doses of kretek smoke on the rat brain. The effects observed in this study were histological of cells abnormalities in the cerebellum. This focus is a continuation of our previous research.^{16,17}

Although Purkinje cell density has been proven histometrically, it is necessary to know the smoke effect of kretek on brain cell histometrics.¹⁶ So, the purpose of this research is to determine the effect of kretek smoke on changes in "rat Purkinje cells". Changes in "rat Purkinje

cells" both qualitatively and quantitatively can be used as a guideline in a more objective diagnosis of brain tissue disorders.

MATERIAL AND METHODS:

Kretek:

The kretek used in this research were made manually with a composition of tobacco, cloves, and sauce is called as "woor". Tobacco, cloves, and sauce were purchased at the market in the Special Region of Yogyakarta, Indonesia.

Measurement of nicotine levels:

Measurement of nicotine levels in kretek used the CAMAG Linomat 5 "Linomat5_220727" S/N 220727 (1.00.13) instrument. The test method used is Thin Layer Chromatography (TLC) Densitometry. The weight of the sample (kretek) used was 500 mg. Nicotine standards were dissolved in ethanol. Nicotine spot density is read at a wavelength of 265 nm. The retardation factor (Rf) value in measuring nicotine levels is 0.64, with a standard of 1010 ug/mL. The formula used to calculate nicotine levels is as follows:

$$\begin{aligned} \text{Nicotin in the sample (ng)} &= \frac{(\text{sample area} - b)}{a} \\ \text{LoD device (ng)} &= \frac{(v2 \cdot b) - b}{a} \\ \text{LoD in sample} &= \frac{\text{LoD device (ng)}}{\text{Number of spottings in the sample (ug)}} \cdot 1000 \\ \text{Sample nicotine levels (ug/g)} &= \frac{\text{Nicotine levels in the device (ng)}}{\text{Number of samples posted (ug)}} \cdot 1000 \end{aligned}$$

Screening GC MS:

The GC-MS tool used to measure the substance content in kretek requires first calibrating the tool. The sample (kretek) was added with 1.5 mL of ethanol in a microtube, then vortexed until homogeneous. Next, the solution was centrifuged at 9500 rpm for 5 minutes. The supernatant is put into a gas chromatography vial, then injected into the gas chromatography column. Column used HP-5ms Ultra Inert Columns.

Ethical clearance:

We obtained the ethical clearance No. 058/KER/FK/IU2024 from the Research Ethics Commission, Faculty of Medicine, Universitas Trisakti, Jakarta, Indonesia.

Animal:

The experimental animals used were the Sprague-Dawley rats. The number of rats is 16, male gender, age: 2 – 3 months, body weight 150 to 200grams, in good health as declared by a veterinarian. During the study, rats were placed in cages individually. Rat cages were placed in an animal treatment room. The room temperature used for these experimental was 24 - 28°C, with a room humidity of 50-60%. The room lighting used

was artificial fluorescence with a light and dark cycle of 12:12 hours. The rats were given food and drink sufficiently (at libitum), based to standards.

Sample size calculated with the minimum sample size formula, namely $N = 10: (2 - 1) + 1 = 5$ rats, while the maximum sample size was $N = 20: (2 - 1) + 1 = 10$ rats.¹⁸ Researchers used 8 rats for each treatment group. Rats were sacrificed after the experiment was completed. Brain organs were taken to make slide preparations.

Treatment:

Acclimatization for 1 week was carried out on all rats included in the study. During acclimatization, rat was in individual cages placed in the animal treatment room. The rats were given food and drink at libitum, according to standards. During acclimatization, rats were not treated. After acclimatization, the rats were randomly grouped into 2 groups, each group consisting of 8 rats. Control group in these studies is CG. CG is rats breathe normal air, not exposed to smoke of kretek. Treatment group in this study is TG, the rats were given treatment, namely exposure to smoke of kretek, with a dose of 1 cigarette/day. The duration of exposure to smoke of kretek on both groups (CG and TG) was 1 month (30 days).

The size of the glass box for treatment is 45 cm long, 35 cm wide and 20cm high (31,500 cm³). The glassbox as a place for cigarette smoke exposure is equipped with a pipe connected to an electric pump. After the kretek is burned, and the electric pump is turned on, the smoke of kretek enters the glass box, then is inhaled by the experimental rats.

Treatment in TG for 10 minutes, every morning for 1 month (30 days). After being treated, the rats were anesthetized to death. We used ketamine (100mg/kg body weight), and xylazine (10mg/kg body weight) intraperitoneally. Animals that had been sacrificed by euthanasia, then their brains were taken, and stored in bottlescontaining 10% neutral buffered formalin (NBF) solution. The next step is that the brains are used to make histological preparations.

Research diagram:

Research diagram is presented in Figure 1.

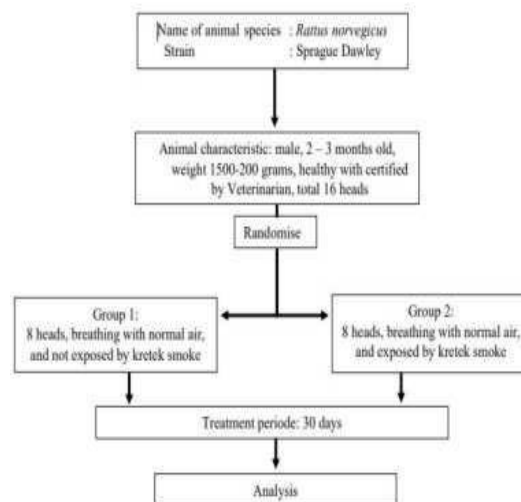


Figure 1. Research flow diagram

Hematoxylin and eosin staining:

NBF 10% is used to fix the brain tissue. Next, the brain tissue was made into slides with hematoxylin and eosin staining as done in previous studies.^{16, 17}

Qualitative observed of Purkinje cells:

Cerebellum slide images were documented using Optilab Advance Plus. Analysis of the slide images used ImageRaster 3. Optilab Advance Plus, and Image Raster 3 devices (<https://miconos.ac.id/new/support/download>). Observation of Purkinje cell abnormalities was shown if abnormalities in cell shape were found. The shape of Purkinje cells between the control group and the treatment group was compared qualitatively.

Quantitative measurement of Purkinje cells:

Cerebellum image documentation has been carried out with Optilab Advance Plus. Quantitative measurement of Purkinje cells was carried out with Image Raster 3 (<https://miconos.ac.id/new/support/download>). Cytometry parameters of Purkinje cells are area, perimeter, length, and width. Three researchers were involved in the measurement of Purkinje cell cytometry. Measurement data are displayed as mean and standard deviation (SD). Independent sample t test was used to compare differences in Purkinje cell cytometry between groups. We used $p < 0.05$ for differences between groups.

RESULTS:

Nicotine levels:

Chromatogram obtained using <win CATS Planar Chromatography Manager= and the standard curve used to measure nicotine levels of kretek are presented in Figure 2.

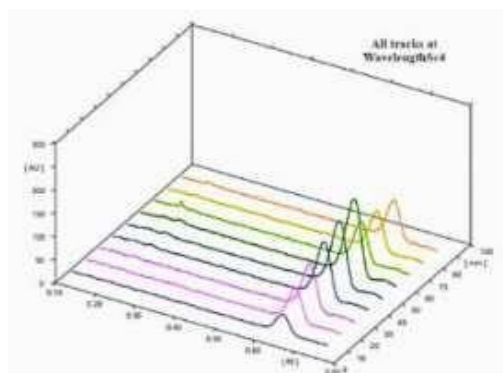
Table 1. Nicotine levels in kretek cigarettes

NS	R	SW (g)	SSV (μ L)	AFS mL	Freq	NDS (μ g)	A	NIS (μ g)	NIDS (μ g/g)	Avr (μ g/g)
1	1	0.5048	2.5	5	1	252.4	5916.1	0.99	3.92	3.92
	2	0.5048	2.5	5	1	252.4	5916.1	0.99	3.92	
2	1	0.5022	2.5	5	1	251.1	5840.5	0.975	3.88	3.84
	2	0.5022	2.5	5	1	251.1	5724.9	0.951	3.79	
3	1	0.5034	2.5	5	1	251.6	5752.6	0.957	3.80	3.80
	2	0.5034	2.5	5	1	251.8	5759.3	0.958	3.81	
4	1	0.5029	2.5	5	1	251.2	5838.4	0.974	3.88	3.88
	2	0.5029	2.5	5	1	251.2	5852.5	0.977	3.89	
5	1	0.5041	2.5	5	1	251.9	5798.4	0.966	3.84	3.91
	2	0.5041	2.5	5	1	251.9	5976.3	1.002	3.98	
6	1	0.5046	2.5	5	1	252.2	5921.2	0.991	3.93	3.93
	2	0.5046	2.5	5	1	252.2	5928.3	0.993	3.94	

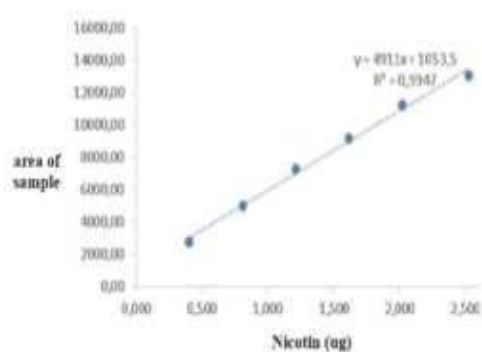
Avr $\pm$ SD 3.88 $\pm$ 0.05

Abbreviations: NS = Number of Sample, R = Replicants, SW = Sample weight, SSV = Sample spotting volume, AFS = Add final sample, F = Frequency, NDS = Number of deep spots, A = area, NIS = nicotine in the sample, NIDS = Nicotine levels in dry samples, Avr = average, g = gram, μ L = micro liter, mL = milli liter, μ g = micro gram, μ g/g = micro gram per gram, SD = standard of deviation.

The nicotine content in kretek used in this study was 3.88 $\pm$ 0.05 μ g/g.



A.



B.

Figure 2. Chromatogram, and Standard curve for nicotine levels.

A. 3-D chromatogram obtained using winCATS Planar Chromatography Manager. B = Standard curve for nicotine levels.

Nicotine levels in kretek cigarettes are presented in Table 1.

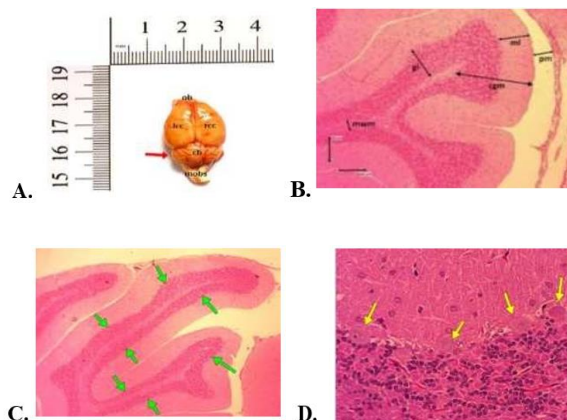
Content of substances in kretek:

Based on the GC-MS chromatogram, there are 99 substances measured in kretek (all types of substances are not shown in this paper). Substances contained in kretek with high amounts including ethyl-

diisopropylacetamide ($C_{10}H_{21}NO$), Pyridine, 2-(1-methyl-2-pyrrolidinyl)- ($C_{10}H_{14}N_2$), 3-Allyl-6-methoxyphenol ($C_{10}H_{12}O_2$), Caryophyllene ($C_{15}H_{24}$), 10-Octadecenoic acid, methyl ester ($C_{19}H_{36}O_2$), 1-Heptatriacotanol ($C_{37}H_{76}O$).

Brain morphology and histological structure of the cerebellum of Sprague Dawley rats:

Brain morphology and histological structure of the cerebellum of rats is presented in Figure 3.

**Figure 3. Brain morphology and histological structure of the cerebellum of rats.**

A, Sprague Dawley rats9 brain. Cerebellum preparations were made in cross sections indicated by red arrows. B. Histology of the cerebellum of Sprague Dawley rats, hematoxylin and eosin staining, objective 10 x. ob = olfactory bulb, rcc = right cerebral cortex, lcc = left cerebral cortex, cb = cerebellum, mobs = medulla oblongata of brain stem, pm = pia matter, ml = molecular layer, cgm = cortex of grey matter, gl = granular cell layer, mwm = medulla of white matter. C. Purkinje cells at the edge of the granular cell layer (green

yellow arrow), hematoxylin and eosin staining, objective 10 x. D. Cell Purkinje (yellow arrow), hematoxylin and eosin staining, objective 40 x.

The brain morphology of Rats looks at the olfactory bulb (ob), left and right cerebral cortex (lcc and rcc), cerebellum (cb), and medulla oblongata of brain stem (mobs). The histological structure of the cerebellum appears in the pia matter (pm), molecular layer (ml), cortex of grey matter (cgm), granular cell layer (gl), medulla of white matter (mwm), Purkinje cells at the edge of the granular cell layer (green yellow arrow). The morphology of the rat's brain between CG was no different compared to TG. Morphologically, the part of the rat's brain between CG was no different compared to TG. All rat brains in this study had the same parts, including ob, lcc, rcc, cb, and mobs.

Qualitative comparison of the cerebellum between treatment groups

Purkinje cells are located at the edge of the granular cell layer of the rat cerebellum in both groups (CG and TG). The appearance of Purkinje cells in CG appears round, while in TG they appear smaller and tapered. Based on this appearance, Purkinje cells in CG appear to have a normal histological structure, while Purkinje cells in TG appear abnormal. A comparison of the appearance of Purkinje cells in rats between groups is presented in Figure 4.

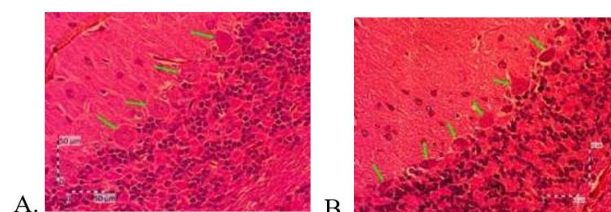


Figure 4. Comparison of the appearance of the Purkinje cells of rats between CG compared to TG. A. Purkinje cells in CG. B. Purkinje cells in TG. Purkinje cells in CG (A) and TG (B) stained with hematoxylin and eosin, and objective 40 x. CG, rats breathe using ordinary air without exposure to smoke of kretek. TG, the group of rats exposed to smoke of kretek 1 stick/day for 1 month (30 days) of treatment. Purkinje cells are indicated by green yellow arrows.

Purkinje cell cytometry:

A cytometry comparison (area, perimeter, length, and width) of the Purkinje cells of rats between CG compared to TG are presented in Figure 5.

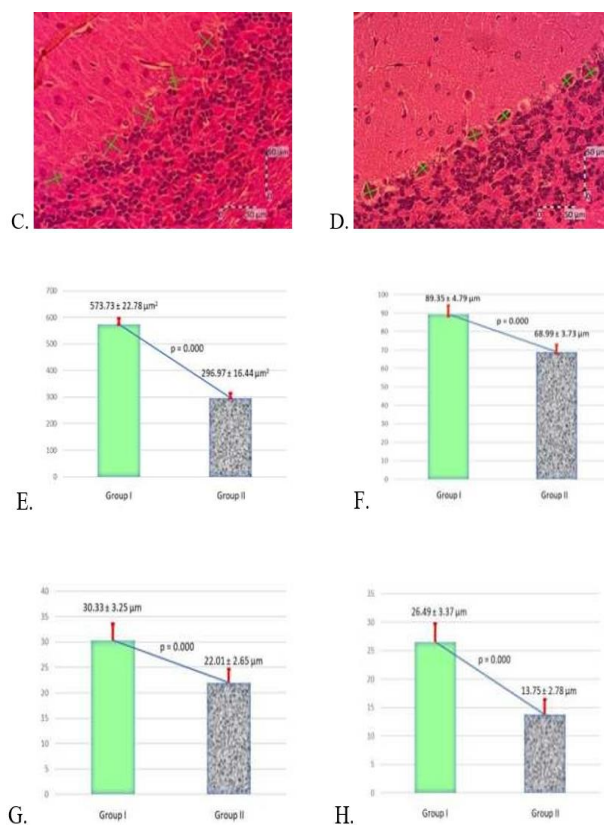
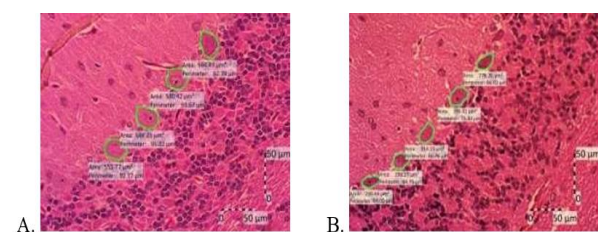


Figure 5. Cytometry comparison of Purkinje cells in rats

A. Area and perimeter of Purkinje cells in CG. B. Area and perimeter of Purkinje cells in TG. C. Length and width of Purkinje cells in CG (control). D. Length and width of Purkinje cells in TG. Purkinje cells in rats were stained with hematoxylin and eosin, 40x objective. E. Area comparison of Purkinje cells between CG compared to TG. F. Perimeter comparison of Purkinje cells between CG compared with TG. G. Length comparison of Purkinje cells between CG compared with TG. H. Width comparison of Purkinje cells between CG compared with TG. CG (control), rats breathe using ordinary air without exposure to kretek smoke. TG, the rat's group that exposed to kretek smoke 1 stick/day for 1 month (30 days) of treatment. Purkinje cells are indicated by green yellow arrows.

Mean value of Purkinje cells area of rats in CG is 573.73 μm², with SD 22.78 μm², number of samples 48, with 95% lower and upper of confidence interval (CI) 567.30 and 579.93 μm², respectively. Mean value of Purkinje cells area of rats in TG is 296.97 μm²; with SD 16.44 μm²; number of samples 48, with 95% lower and upper of CI 292.46 and 301.79 μm², respectively. Levene's test for equality of variances of Purkinje cells area with F value 4.704; p = 0.033; p value of t-test for equality of means 0.000; with t = 68.26; df = 85.51. Purkinje cells area of rats in CG was higher than TG (p = 0.000).

Mean value of Purkinje cells perimeter of rats in CG is 89.35 μm , with SD 4.79 μm , number of samples 48, with 95% lower and upper of CI 87.98 and 90.63 μm , respectively. Mean value of Purkinje cells perimeter of rats in TG is 68.99 μm ; with SD 3.73 μm ; number of samples 48, with 95% lower and upper of CI 67.93 and 70.02 μm , respectively. Levene's test for equality of variances of Purkinje cells area with F value 2.70; $p = 0.104$; p value of t-test for equality of means 0.000, with $t = 23.24$; $df = 94$. Purkinje cells perimeter of rats in CG was higher than TG ($p = 0.000$).

Mean value of Purkinje cells length of rats in CG is 30.33 μm , with SD 3.25 μm , number of samples 48, with 95% lower and upper of CI 29.43 and 31.23 μm , respectively. Mean value of Purkinje cells length of rats in TG is 22.01 μm , with SD 2.65 μm , number of samples 48, 95% lower and upper of CI 21.27 and 22.79 μm , respectively. Levene's test for equality of variances of Purkinje cells area with F value 3.79; $p = 0.054$, p value of t-test for equality of means 0.000, with $t = 13.75$; $df = 94$. Purkinje cells length of rats in CG was higher than TG ($p = 0.000$).

Mean value of Purkinje cells width of rats in CG is 26.49 μm , with SD 3.37 μm , number of samples 48, with 95% lower and upper of CI 25.56 and 27.38 μm , respectively. Mean value of Purkinje cells width of rats in TG is 13.75 μm , with SD 2.78 μm , number of samples 48, with 95% lower and upper of CI 12.95 and 14.56 μm , respectively. Levene's test for equality of variances of Purkinje cells width with F value 1.033, $p = 0.312$, p value of t-test for equality of means 0.000, with $t = 20.21$, $df = 94$. Purkinje cells width of rats in CG was higher than TG ($p = 0.000$).

DISCUSSION:

The nicotine content in kretek used in this study was $3.88 \pm 0.05 \mu\text{g/g}$. It has been shown that tobacco use is associated with nicotine dependence.¹⁹ It has been proven that nicotine causes addiction in users.²⁰ The consequence of a smoker is that the nicotine levels in the body increase. Although there are other alternatives in the form of electronic cigarettes which are intended to reduce nicotine levels.^{21,22,23} However, it is important to note that e-cigarettes can also use nicotine as a vaporizable substance.²⁴ Reducing nicotine levels in kretek needs to be done because it has the potential to provide benefits to public health.^{25,26, 27} Despite the occurrence of hyperexcitability reactions,²⁸ smoking cessation is better for maintaining better health. Therefore, nicotine replacement therapy (NRT) is needed to replace nicotine from cigarettes used by smokers.²⁹ It has been clearly stated that cigarettes cause health problems not only in the respiratory tract but also in body organs up to the molecular level, for example in

antioxidant enzymes.³⁰ Regarding the substance content in kretek, in this study, we did not measure eugenol levels. The results of other studies demonstrate that the eugenol levels in kretek range from 2.8-33.8 mg/stick.⁶

There are several substances in kretek that are contained in high amounts, including Pyridine, Caryophyllene (C₁₅H₂₄), methyl ester (C₁₉H₃₆O₂), and 1-Heptatriacotanol (C₃₇H₇₆O). Apart from that, there are also molecules of ethyl-diisopropylacetamide (C₁₀H₂₁NO), 3-Allyl-6-methoxyphenol (C₁₀H₁₂O₂), 2-(1-methyl-2- pyrrolidinyl)- (C₁₀H₁₄N₂), and 10-Octadecenoic acid. Although we did not check eugenol levels, the kretek used in this study contained caryophyllene. We know that caryophyllene is an essential herbal oil, including clove oil. Caryophyllene has been proven to be anti-inflammatory by inhibiting key inflammatory mediators, for example inducible Interleukin 1 beta (IL-1 β) and nitric oxide synthase (iNOS).^{31, 32} Pyridine and its derivatives are heterocyclic compounds with low molecular weight. Even though our research results show high levels in cigarette smoke, pyridine is used as an anti-oxidant and anti-bacterial. Apart from that, pyridine is also used to treat various diseases, for example cardiovascular disease, anti-cancer, and anti-coagulant.³³ Based on the results of previous studies, we suggest that further research be conducted on the relationship between the content of substances in kretek and macrophage recruitment as an inflammatory response due to exposure to cigarette smoke.³⁴

Fatty acid methyl esters (FAME) occur through the transesterification process of fat with methanol. FAME is found for example in biodiesel, usually obtained from vegetable oils through transesterification. Apart from that, FAME is also used to produce detergents and biodiesel.³⁵ Although it has been demonstrated that there is a correlation between fatty acid metabolic pathways and acute lung injury.³⁶ Because the high fatty acid content in kretek is a source of exposure to lung organs, in the future research needs to be focused on the fatty acid aspect of lung injury, as well as other organs. Heptatriacotanol molecules are also contained in kretek. Heptatriacotanol acts as an anti-oxidant, anti-inflammatory, and anti-cancer.³⁷

In this study, Sprague Dawley's brain exposed to kretek smoke with low doses appeared normal, and did not differ morphologically compared to the group that was not exposed (CG as a control group). Exposure to kretek smoke with low doses, namely 1 stick/day for 1 month (30 days), did not affect Sprague Dawley's brain morphology. We compared the brain morphology of rats qualitatively. When compared with the results of previous studies, the morphology of the rat brain in this

study appears to be the same size. Moreover, it is also shown that the cerebrum appears to be the largest part of the rat brain. The olfactory bulb is in the rostral part of the cerebrum, while the caudal part of the cerebrum is the cerebellum, and the ventral part is the brainstem.^{38,39}

Changes in the shape of Purkinje cells in the cerebellum of rats exposed to smoke of kretek 1 stick/day for 1 month (30 days) showed abnormalities. The Purkinje cell abnormalities in this study were like brain abnormalities in rats exposed to tobacco smoke for a long time. Previous research demonstrated that in adult rats exposed to very low doses of tobacco smoke for a long time found a reduction in immature neurons in the brain.⁴⁰ Although our previous research has not measured Purkinje cell cytometry, our study showed that exposure to smoke of cigarette 1 stick/day for 3 months decreased Purkinje cell density (in the cerebellar cortex).¹⁶ These abnormal Purkinje cells are a sign of degeneration. Purkinje cells change size and shape, from large and round to smaller and tapered (Figure 5). The occurrence of pathological conditions of Purkinje cells in this study is in line with the oxidative stress theory. This Purkinje cell condition occurs due to oxidative stress. Oxidative stress can originate both exogenously and endogenously. Cigarette smoke contains chemical compounds that trigger compounds in cells to form proinflammatory compounds. The modulation that occurs in these intracellular proinflammatory pathways results in pathological conditions.⁴¹ This fact is reinforced by research results that demonstrate cigarette smoke causes inflammation with various mechanisms of action.^{42, 43}

The results of this research, which show a cytometry decrease in Purkinje cells in a TG are in line with the results of previous research. Previous research results that are in accordance with the results of this study include the nicotine content in tobacco. Research results have demonstrated that apart from nicotine, tobacco also contains alkaloids and other secondary metabolites.⁴⁴ In more detail, cigarettes purchased on the market contain about 1.5% alkaloids by weight of tobacco. Tobacco contributes about 95% of the total alkaloid content.⁴⁵ It has been demonstrated that the nicotine in cigarette smoke decreases brain volume. It was further shown that individuals who actively smoke daily were strongly associated with a decrease in total grey matter. In more detail it was demonstrated that increasing the smoking dose had a greater effect on reducing brain volume.⁴⁶ It is not just the smoke effect of kretek on the brain, it has been further demonstrated that smoke of kretek also affects the brain reward threshold. The results of previous research on rats exposed to nicotine at various concentrations per cigarette (0.028; 0.07; 0.13; 0.272; and 0.84 mg/stick) showed that nicotine lowered the brain reward threshold.⁴⁷

Previous research results show that nicotine in tobacco has a serious impact on the body through various multidimensional pathways. Apart from that, nicotine also has an impact on nerve health. The exact mechanism of nicotine's effect on nerve health is not yet known.⁵ The influence of nicotine in cigarette smoke on neurological health is certainly related to the decreased in Purkinje cell cytometry in the results of this study. The reduction in Purkinje cell cytometry in the results of this research is in line with the results of previous studies. The results of previous research demonstrated that smoking decreased grey matter volume (GMV) in most brain areas. The GMV measurement was carried out using voxel-based morphometry (VBM). The results of this study also shown that cigarette smoke reduces GMV in the cerebellum.⁴⁸ Our results are in line with other studies showed that exposure to kretek smoke can impact brain structure and function.⁴⁹ Moreover, it has been shown that low dose cigarette smoke exposure also demonstrated of overexpression of p53 gene.¹⁰

Purkinje cell abnormalities in the group of mice exposed to cigarette smoke need to be compared with the control group, this is important in histopathology. Changes in Purkinje cell size include changes in area, perimeter, length, and width. The appearance of abnormal Purkinje cells is characterized by a smaller size than normal ones, so that the area, perimeter, length, and width are also reduced. Likewise, the tapered appearance of Purkinje cells also shows that the size of the area, perimeter, length, and width decreases. Quantitative changes to Purkinje cells (area, perimeter, length, and width) affect the qualitative appearance of the cells. Based on the cerebellum is a brain region that plays an important role in motor control,¹² then in the future it is necessary to investigate the relationship between Purkinje cell abnormalities and motor function.

LIMITATION:

The limitation of this research is that we did not measure the substance content in kretek smoke, for example levels total alkaloids, tar, and eugenol. These substances certainly affect the cerebellum of mice, especially the occurrence of Purkinje cell abnormalities. We also did not correlate the levels of substances in kretek smoke with the degree of Purkinje cell abnormalities. Apart from that, we also did not measure the thickness of each layer of the cerebellum, the characteristics of the cells in the granule cell layer of the cerebellum. Abnormalities in the size and shape of Purkinje cells which are associated with motor function are important to study because they can be used in diagnosis both at the cellular and tissue levels.^{50,51}

CONCLUSION:

Exposure to low doses of kretek smoke of 1 stick/day for 1 month (30 days) in rats did not affect morphological changes in the brain. Kretek smoke 1 stick/day for 30 days reduces the size of Purkinje cell bodies and changes the shape from round to tapered. In the future, it is necessary to investigate the clinical implications of Purkinje cell abnormalities on motor function due to kretek smoke exposure. More specifically, it is necessary to examine abnormalities in the size and shape of Purkinje cells that experience degeneration due to kretek smoke exposure.

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CONFLICT OF INTERESTS:

All authors declare that there is no conflict of interest.

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ETHICAL STATEMENT:

Ethical approval for this research is Number: 058/KER/FK/IU2024 by the Research Ethics Commission, Faculty of Medicine, Universitas Trisakti, Jakarta, Indonesia.

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AUTHORS CONTRIBUTIONS:

DT, EP, HJE = Schemed, and designed experiment. DV, HJE, EP, AVO, SK = data collecting, analysis, and the results interpretation. EP, JJNT, LG, HJE = images review, and processing. DV, HJE, EP, SK = preparation of writing a manuscript. All author9s = reviewing and approved the final manuscript.

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