About the Journal

Focus and Scope

Pharmacy Education journal provides a research, development and evaluation forum for communication between academic teachers, researchers and practitioners in professional and pharmacy education, with an emphasis on new and established teaching and learning methods, new curriculum and syllabus directions, educational outcomes, guidance on structuring courses and assessing achievement, and workforce development. It is a peer-reviewed online open access platform for the dissemination of new ideas in professional pharmacy education and workforce development. *Pharmacy Education* supports Open Access (OA): free, unrestricted online access to research outputs. Readers are able to access the Journal and individual published articles for **free** - there are no subscription fees or 'pay per view' charges. Authors wishing to publish their work in *Pharmacy Education* do so without incurring any financial costs.

In addition we are listed in EBSCO, and indexed in the Emerging Sources Citation Index (ESCI - Web of Science), EMBASE and SCOPUS.

The Journal also recognises the importance of policy issues and current trends in the context of education, professional development and workforce.

The Journal publishes reports of research and innovation in all aspects of professional pharmacy education and training, case studies, country studies, innovations in laboratory and professional educational practice, workforce issues and development, reviews and reports on information technology in education and reviews of current literature.

The Journal has a clear international perspective, and has a longstanding policy of facilitating publication, in particular for younger Faculty, and those authors whose first language may not be English, and manuscripts from all regions seeking low cost engagement with the wider global community.

The Journal is published by the International Pharmaceutical Federation (FIP) and is aligned to the global mission of advancing education, advancing practice and advancing science.

Peer Review Process

Pharmacy Education has adopted a double-blind peer review process - the identities of the Authors and Reviewers are kept from being known to each other. A step-by-step checklist is provided for Authors, Reviewers and Editors to ensure this (see Ensuring a Blind Review).

Peer Review Process: Once a submission is received, the assigned Editor will select appropriate Reviewers based on their expertise and proven ability to critique. The peer reviews received will assist the Editor in determining the validity, significance and originality of the work submitted. Reviewers will also provide comment on manuscript content for scientific value, check for adherence to general scientific practice as well as *Pharmacy Education's* specific guidelines. The Peer Review process will look closely at methodology and the data validity, and consider the ethical approach. Reviewers are encouraged to provide suggestions for improvement and recommend to Editors if manuscripts should be accepted, accepted with revisions, or rejected.

Please note that an invitation for Authors to submit a revised version is not a guarantee of acceptance. Ultimately, the final decision lies with the Editor assigned to each submission. An Editor can reject any article at any time before publication, including after acceptance if concerns arise about the integrity of the work.

As part of their agreement with *Pharmacy Education,* Reviewers will keep manuscripts and associated material strictly confidential, and will not appropriate Authors' ideas before the manuscript is published. Once a review has been completed, Reviewers will be directed and expected to permanently delete/destroy any retained copies of manuscripts they hold (see Privacy Statement).

Timeliness: Reviewers are expected to respond promptly to requests to review and to submit reviews within the time agreed. Reviewers are also required to declare their conflicts of interest and recuse themselves from the Peer Review process if a conflict exists. Editors will do their utmost to ensure timely processing of manuscripts. Authors will be notified on any unusual delays in publication of manuscripts via email. Authors will ne notified as soon as possible if a manuscript is going to be rejected, either by the Journal Manager or Editorial Team.

Journal Ownership and Editorial Scope

Pharmacy Education is published by the International Pharmaceutical Federation (FIP). Appointments and dismissals to the Editorial Team are made by the Editor-in-Chief in consultation with FIP.

Editorial roles and responsibilities

Editor-in-chief - The Editor-in-Chief has full authority over content publication in *Pharmacy Education.* In co-operation with the wider Editorial Team and publisher, they direct overall strategy of the journal. Together with the Editors and Associate Editors, the Editor-in-Chief reviews and decides upon submitted manuscripts, ensuring timely publication of submissions.

Editors and Associate Editors – Editors and Associate Editors are appointed for a three (3) year term to the Editorial Team. Their responsibilities include, but are not limited to, decision making based on peer review feedback, recommending appointments to the Reviewer Board, and responding to editorial enquiries.

Advisory Board – *Pharmacy Education* is currently engaged in establishing an Advisory Board who alongside the Editor-in-Chief, Editors and Associate Editors will assist with:

- Guidance on the peer review and publishing policies of Pharmacy Education and where necessary, suggest reviewers to the Editor-in-Chief.

- Developing the journal by providing expertise to the Editor-in-Chief and FIP on how to increase impact and reach

- Impartial Judgement in appeal cases by providing professional, independent scientific comments to the Editor-in-Chief and FIP

- Promoting *Pharmacy Education*

Managing Editor – The Managing Editor assumes day-to-day responsibility of managing the submissions flow to *Pharmacy Education*. They liaise with Authors and Reviewers where needed, clarifying the Submission and Publication process as well as responding to all general enquires. The Managing Editor also completes all typesetting, proofreading and online publication of accepted manuscripts once accepted by the Editors.

Advertising in Pharmacy Education

Pharmacy Education does not provide opportunities for advertising on any of its platforms, including downloadable content. This policy maybe reviewed in future in conjunction with the publisher, FIP.

Competing Interest Guidelines

To assist *Pharmacy Education* in ensuring public trust in the scientific process and the credibility of articles that it publishes, all those involved in the Submissions and Peer Review process are required to disclose perceived as well as actual conflicts of interest.

Authors: When submitting an article to *Pharmacy Education*, all Authors are required to disclose all financial and personal relationships that may bias their work (see Submission Preparation Checklist)

Peer Reviewers: Reviewers are asked at the time of conducting a review if they have conflicts of interest that may impact on their ability to provide an unbiased review. Reviewers are asked to disclose conflicts of interest to the assigned Editor. The assigned Editor will then cancel the review and reassign the article to another reviewer. Reviewers agree to not use knowledge of the work they are reviewing before its publication to further their own interests.

Editors and Journal Staff: Editors making final decisions on manuscripts will recuse themselves where conflicts of interest or relationships that pose potential conflicts are present. All editorial staff (including guest editors) provide the Editor-in-Chief with a completed Editorial Disclosure Form (up to date description of financial interests/conflicts). Editors will annually publish disclosure statements about potential conflicts of interests related to the commitments of journal staff.

Research involving Human participants and Informed Consent

It is the responsibility of the authors to ensure that research involving human subjects has been reviewed and approved by the appropriate research or ethics review committee, or that it has been determined to be exempt from such review.

Confirmation of this should be included in the Cover Letter and also included in the Methods section of the manuscript. Where informed consent is required, authors should include a statement in the manuscript detailing that informed consent was obtained from human subjects (see Submission Preparation Checklist)

Article Corrections, Replacement, Retractions & Removal Policy

Published articles are a permanent record that should remain unaltered. However, *Pharmacy Education* recognises that in exceptional circumstances, articles may need to be corrected, replaced, retracted or removed.

The Editor-in-Chief has full authority over content publication in *Pharmacy Education*. In making decisions regarding publication, the Editor-in-Chief is guided by the policies of the Journal as well as legal requirements such as libel, copyright, infringement and plagiarism.

Corrections

Detailed below are our procedures for managing requests for corrections post publication

Minor errors

If Authors identify a minor error once an article has been published online, they are advised to email their request for corrections to *Pharmacy Education* for consideration.

Minor errors include: errors in spelling, data, medical terms; missing text; amendments to tables, figures or appendices; errors in correspondence details, etc. The Journal may decline proposed corrections that are for aesthetic reasons; errors to text, typography tables, figures and appendices if the meaning is unchanged; errors in acknowledgments lists *etc*.

Significant Corrections

Corrections may be needed if honest errors have resulted in a portion of an article being misleading; if the author/contributor lists are disputed; or if potential conflicts of interest affecting authorship are disclosed post publication.

Where the Editor-in-Chief agrees that a correction is needed, the Journal will:

- Correct the error online, and to any article file for download, linking to a **Correction Notice** via a footnote

- The **Correction Notice** will detail the changes made to the original version, and the dates the changes were made.

Replacement

Honest errors such as mis-classification or miscalculation may lead to significant changes to the results, interpretations and conclusions. In such cases, the Journal will consider retraction with replacement of the article:

- The changed version of the article will undergo further editorial review;

- The authors will be required to detail and explain the changes made which will be published as supplementary material or in an appendix;

- The supplementary material/appendix will be attached to the changed version, allowing for complete transparency.

Retraction

An article will be retracted if the results or conclusions are unsound and/or where misconduct breaching professional ethical codes has occurred. The publisher and Editor-in-Chief will conduct an investigation into the errors or misconduct before retracting an article. The following steps will be taken where articles are retracted:

- A **Statement of Retraction**, giving the reasons for the retraction and signed by the authors and/or the Editor-in-Chief will be published online linking to the original article.

- The original article is preceded by a screen containing the **Statement of Retraction**. The reader can then proceed to the article itself.

- A watermark will be added to the original PDF indicating on each page that it is “RETRACTED”

- The **Statement of Retraction** will be included as a numbered page in the Table of Contents to ensure proper indexing, and will include the article title in its heading

Removal

Very occasionally, it may be necessary to remove an article from the online database as a consequence of legal action (*e.g.*, defamatory content, infringement on legal rights, article is subject of a court order, or might pose a serious health risk if an article's content is acted upon).

In these circumstances:

- The article's metadata (title and author details) will be retained and the text replaced with an **Article Removal Notice**

- The **Article Removal Notice** will be included in the Table of Contents and prefix the metadata.

Expressions of Concern

If concerns or allegations of misconduct regarding a publication are raised, the Editor-In-Chief will consult the Committee on Publication Ethics (COPE) http://www.publicationethics.org and initiate the appropriate procedure based on the nature of the concern or allegation. The Editor-in-Chief, with appropriate support form the Editorial Team, will assess each situation individually.

The Editor-in-Chief will consider issuing an **Expression of Concern** if:

- the Editor judges that readers should be made aware of potentially misleading information contained in a published article;

- investigations into any concerns of misconduct remain inconclusive;

- concerns remain over the impartiality of any investigations into alleged misconduct;

-an investigation is pending and a judgment is not expected for some time.

An **Expression of Concern** will be published and appear in the Table of Contents and include the title of the article in its heading. It should be noted that *Pharmacy Education* understands the potential repercussions that issuing an **Expression of Concern** can bring and will only take this action where it is deemed necessary.

If an investigation produces evidence of misconduct or reveals that the concerns raised are well founded after an **Expression of Concern** has been published, the Journal will instigate the Retraction process

Appeals and Complaints

Appeals

Authors are entitled to appeal editorial decisions if they believe their submission has been unfairly or inappropriately rejected. An appeal letter should be submitted to the Journal Manager (pej@fip.com)

The appeal letter should provide appropriate detail and context. For example, if an Editor has provided peer review comments it is worthwhile responding to each item in the letter. If the appeal is against the editorial decision made on the submission, explaining and justifying clearly the work's importance, relevance, and usefulness in the appeal letter is recommended.

An invitation to submit a revised version after sending an appeal letter does not guarantee acceptance; the revised article will proceed through the Peer Review process again.

Appeal letters will be ordinarily acknowledged within 5 working days, followed by a full response containing the appeal decision within 4 weeks.

Complaints

Pharmacy Education aims to respond quickly, courteously, and constructively to complaints about the Journal's procedures, policies, or actions.

Complaints will be considered if:

- the complainant defines their dissatisfaction as a complaint; *and*

- it concerns a failure of process, *i.e.* a long delay or a severe misjudgement; and is not simply disagreement with an editorial decision;

- the issue being raised is within the responsibility of *Pharmacy Education*'s editorial remit

Complaints should be directly emailed to the Journal Manager (pej@fip.com) who will ordinarily formally acknowledge receipt within 5 working days.

- The Journal Manager will forward the complaint to a relevant person within the Journal organisation who will aim to provide a full response within four weeks. If this is not possible, an interim response and update will be given within the four weeks.

- Following this action, if the complainant remains unhappy, complaints will be escalated to the Editor-in-Chief whose decision is final.

- If a complainant remains unhappy, they may complain to an external body such as the **Committee on Publication Ethics** (COPE) http://www.publicationethics.org. They will consider complaints against Editors once a Journal's own Complaints procedures have been exhausted.

Whistleblowing

Pharmacy Education recognises that there may be legitimate reasons for individuals who wish to remain anonymous when raising issues relating to publication ethics. Concerns or allegations raised anonymously will be handled as they would be if the complaint were from another source, following the processes and procedures of the Journal.

If concerns remain after processes have been followed, The Editor-in-Chief will seek advice from **Committee on Publication Ethics** (COPE) http://www.publicationethics.org

Sponsors

Pharmacy Education is kindly assisted by the following organisations.

- University College London, School of Pharmacy
- University of Namibia, School of Pharmacy
- Monash University, Faculty of Pharmacy and Pharmaceutical Sciences
- UNESCO UNITWIN

Sources of Support

FIP Education Initiative

Journal History

Pharmacy Education has been publishing peer reviewed education, training, research and evaluation in the field of pharmaceutical education since 2000.

The Journal encourages manuscript submissions from younger career scientists, academics and practitioners and has a focus on supporting authors who do not have English as a first language.

Through our FIP publication platform we are able to reach out to over 3 million pharmacists and pharmaceutical scientist worldwide.

ISSN: 1477-2701

Vol. 21 No. 2 (2021): IAI Conference 2020

We are pleased to confirm the publication of IAI Conference 2020.

Published: 28/07/2021

Conference Proceedings

PDF

IAI CONFERENCE: In vivo activity of Phaseolus vulgaris as an anti-hypercholesterolemic

Keni Idacahyati, Yedy Purwandi Sukmawan, Nopi Yanti, Winda Trisna Wulandari, Firman Gustaman, Indra

p. 184-188

PDF

IAI CONFERENCE: Comparing the quality of life of neuropathic patients treated with gabapentin and pregabalin at the neuropathic poly of the NTB provincial hospital in 2019

Nurul Qiyaam, Baiq Leny Nopitasari, Haerul Muhajiji

p. 225-229

PDF

IAI CONFERENCE: The comparison of the actual cost to case-mix of type 2 diabetes mellitus inpatient in Pandan Arang Boyolali hospital

Sri Bintang Sahara Mahaputra Kusuma Negara, Devi Ristian Octavia, Primanitha Ria Utami

p. 269-274

PDF

IAI CONFERENCE: Adverse drug reactions associated with successful treatment of multidrug-resistant tuberculosis patients in Cempaka Putih Islamic Hospital Central Jakarta

Adin Hakim Kurniawan, Harpolia Cartika, Siti Aisyah

p. 15-21

PDF

IAI CONFERENCE: Correlation between the level of knowledge of drug managers and drug management in several primary health centres in Malang regency

Ayuk Lawuningtyas Hariadini, Nur Ishmah, Hananditia Rachma Pramestutie

p. 61-66

PDF

IAI CONFERENCE: The potential of banana fruit Ranggap (Musa paradisiaca var. Troglodytarum) as an excipient alternative to oral tablet dosage form

Dolih Gozalil, Iyan Sopyan, Resmi Mustarichi, Wahyu Priyo Legowo

p. 98-107

PDF

PDF

IAI CONFERENCE: The effect of biofilm formation on the outcome therapy of diabetic foot infections (DFIs) patients in the outpatient clinic and inpatient ward of Dr Sardjito General Hospital Yogyakarta

Ika Puspitasari, Titik Nuryastuti, Rizka Humardewayanti Asdie, Hemi Sinorita, Nusaibah Umaroh4, Wahyu Tri Hapsari

p. 172-177

PDF

IAI CONFERENCE: Effectiveness of combination of Moringa Leaf Extract (Moringa oleifera Lamk.) and Papaya Seed Extract (Carica papaya L.) in reducing blood sugar levels of diabetic rats

Novi Ayuwardani, Yetti Hariningsih

p. 215-219

PDF

IAI CONFERENCE: Antiseptic gel formulated from ethanol extract of Citronella grass (Cymbopogon nardus) using CMC-Na, arabic gums, and gelatin as gelling agents

Reynelda Juliani Sagala, Lorensia Yolanda, Michael

p. 258-263

PDF

IAI CONFERENCE: Drug interactions in patients with hypertension at Persahabatan hospital in 2015

Zainul Islam, Atika Vitasari, Muhammad Arif Ridwan

p. 309-314

PDF

IAI CONFERENCE: Analysis of pharmacists' knowledge and attitude in the pharmaceutical industry of halal certification and their readiness to produce halal medicine

Abdul Rahem, Mustofa Helmi Effendi, Hayyun Durrotul Faridah

p. 1-7

PDF

IAI CONFERENCE: The evident gap between actual and perceived facilities supporting value-added pharmacy services

Andi Hermansyah, Catur Dian Setiawan, Firqin Fuad Riansyah

p. 48-51

PDF

IAI CONFERENCE: Formulation and physical evaluation of facial cream preparations from Ceremai fruit juice (Phyllanthus acidus (l.) Skeels)

Danang Indriatmoko, Nani Suryani, Tarso Rudiana, Mila Kurniah

p. 87-92

PDF

IAI CONFERENCE: Acute toxicity study of the ethanolic extract of Eleutherine bulbosa Urb in Wistar rats

Helmina Wati, Rahmi Muthia, Kartini, Finna Setiawan

p. 143-147

PDF

IAI CONFERENCE: Microencapsulation of Jeringau Rhizome essential oils (Acorus calamus L.) using β-Cyclodextrin

Ledianasari, Deby Tristiyanti, Elva Maulydha Tanjung, Lovelyta Barani

p. 189-194

PDF

IAI CONFERENCE: Analysis of white pepper essential oil components using gas chromatography-mass spectroscopy

Purwaniati, Gilang Eka Permana, Indro Pamudjo

p. 230-234

PDF

IAI CONFERENCE: Role of pharmacist in providing drug information and education for patients with chronic diseases during Transition of Care

Umi Athiyah, Abdul Rahem, Catur Dian Setiawan, Andi Hermansyah

p. 275-280

PDF

IAI CONFERENCE: The effect of ethanol extract from Portulaca oleracea on inhibiting total cholesterol on animal subjects

Afifah Bambang Sutjiatmo, Fahmy Ahsanul Haq, Sulaeman Al Jati, Suci Nar Vikasari

p. 22-26

PDF

PDF

IAI CONFERENCE: Hypoglycemic activity test on smooth pigweed (Ammaranthus Hybridus L) leaf water extract on male Wistar rats

Asti Yunia Rindarwati

p. 56-60

PDF

IAI CONFERENCE: The potential effect of the green coffee extract on reducing atherogenic index in hyperlipidemic rats

Fransiska Maria Christianty, Fifteen Aprila Fajrin, Andrean Roni

p. 126-131

PDF

IAI CONFERENCE: The effect of loss-of-function allele (CYP2C19*3) with Clopidogrel efficacy in coronary heart disease patients

Ike Dhiah Rochmawati, Nur Hidayat, David Pomantow

p. 178-183

PDF

IAI CONFERENCE: Activity test of fruit and pomegranate seeds (Punica granatum l) as a hepatoprotector against white male Wistar rats

p. 220-224

PDF

IAI CONFERENCE: Mother's knowledge and practices towards self-medication of fever among children under five years in Muncar Banyuwangi, Indonesia

Sinta Rachmawati, Khusnul Khotimah, Ika Norcahyanti

p. 264-268

PDF

ADVANCING PHARMACY WORLDWIDE

ISSN: 1477-2701

Pharmacy Education (2021) 21(2) 108 - 115
https://doi.org/10.46542/pe.2021.212.108115

IAI CONFERENCE

RESEARCH ARTICLE

Correlation between the antioxidant capacity of plasma and blood glucose level

Eva Nurinda[1], Emelda[2], Nurul Kusumawardani[3]

[1]Department of Pharmacology, Alma Ata University, Bantul, Yogyakarta, Indonesia

[2]Department of Herbal Pharmacy, Alma Ata University, Bantul, Yogyakarta, Indonesia

[3]Department of ClinicalPharmacy, Alma Ata University, Bantul, Yogyakarta, Indonesia

Keywords
Antioxidants
Blood glucose
Diabetes mellitus
Total antioxidant capacity

Correspondence
Eva Nurinda
Department of Pharmacology
Alma Ata University
Brawijaya Road no.99 Jadan
Tamantirto
Bantul
Yogyakarta 55183
Indonesia
evanurinda@gmail.com

Abstract

Introduction: Oxidative stress on tissues can cause diseases such as diabetes mellitus (DM). **Aim:** This study aimed to pharmacologically evaluate the decrease in blood glucose levels and its relationship with the total antioxidant capacity of the blood compared to glibenclamide. **Method:** An experimental study with completely randomised designs was carried out. Rats were induced with streptozotosin followed by ethanolic extract for ten days. **Results:** The One-Way Anova test, showed that the increase of the total antioxidant capacity of plasma treated with ethanolic extract of *Tinospora cordifolia* and *Curcuma zanthorrhiza* was comparable in the same amount to glibenclamide (p=0.345), (p=0.289). There was a relationship between total blood antioxidant capacity and blood glucose levels, this linear association was expressed with the following mathematical equation: y = 20,253 - 2,946x. **Conclusion**: The antioxidant content of *Tinospora cordifolia*, *Curcuma zanthorrhiza*, and *Cinnamomum verum* has the potential to control blood glucose in diabetes mellitus.

Introduction

Diabetes mellitus can be caused by oxidative stress and oxidative damage in tissues. These can also cause other diseases such as atherosclerosis or rheumatoid arthritis. Patients with type 2 diabetes mellitus often have various tissues affected by oxidative stress, including pancreatic β cells (Tangvarasittichai, 2015).

Glucose can be oxidized before binding to proteins, as glycated proteins can be oxidized to produce reactive oxygen species (ROS) (Tiganis, 2011). Hyperglycemia exacerbates the formation of ROS by several mechanisms. ROS increase the expression and formation of tumour necrosis factor- α (TNF- α) and exacerbate oxidative stress. TNF-α can cause insulin resistance in many ways, such as by decreasing the autophosphorylation of insulin receptors, changing the substrate for insulin receptor 1 to inhibit insulin receptor tyrosine kinase activity, decreasing the sensitivity of glucose insulin transporter (GLUT-4), increasing the circulation of fatty acids, changing its function, ß cells and increasing triglyceride levels and by decreasing HDL levels. Previous studies have shown that TNF-α injection in healthy test animals will reduce insulin sensitivity due to hyperglycemia without decreasing plasma insulin levels (Dewanjee *et al.*, 2018).

Antioxidants can decrease free radical levels as proved by Luo and the authors (2019), and thereby reducing insulin resistance (Luo *et al.*, 2019). Antioxidants can decrease reactive oxygen species (ROS), which as a result reduces oxygen which will bind to free electrons released due to the electron chain leak. The reaction

between oxygen and free electrons produces ROS in mitochondria (Annisa *et al*., 2014).

Secondary metabolites found in plants can act as antioxidants; an example of these are flavonoids. Flavonoids derived from vegetables and medicinal plants have beneficial effects on diabetes by improving glycemic control, lipid profile, and antioxidant status. The antioxidants in flavonoids can donate their hydrogen atoms. Flavonoids will be oxidized and bind to free radicals so that the free radicals become more stable compounds (Ghorbani, 2017).

Several studies have been conducted on Indonesian herbs that are used for anti-diabetes in order to study their antioxidant activity. Most of these studies were conducted *in vitro*, such as a study conducted by Rui Wang, in which he examined the composition of volatile compounds in five species of cinnamon. In his research, it was known that the cinnamon antioxidant activity was 45.42% by using the DPPH method (Wang *et al.*, 2009). Cinnamon twig bark has the highest antioxidant activity compared to bark and branches assayed semiquantitatively by using the DPPH method (Ervina *et al*., 2016). The standardized extract of *Curcuma xanthorrhiza* and the active component *Xanthorrizol* significantly weakened the induction of a high-fat diet (HFD) against hyperglycemia and insulin resistance (Kim *et al*., 2014). Puranik conducted a study looking at the antidiabetic activity of *Tinospora cordifolia*. According to his study, *Tinospora cordifolia* had significant antidiabetic activity in diabetic rats by 40% to 80% compared to insulin (Puranik *et al*., 2010). Another plant that has antidiabetic potential is *Averrhoa bilimbi L* because its leaves contain flavonoids. Flavonoids function as antioxidants and antidiabetics (Alhassan & Ahmed, 2016). In previous studies that examined flavonoids in several Indonesian plants, researchers wanted to evaluate the pharmacological decrease in blood glucose levels by using herb extract. Its relationship with the total antioxidant capacity of the blood was studied and compared with glibenclamide which is widely used in diabetic treatment.

Materials and methods

Extract preparation

The extractions of *Cinnamomum zeylanicum*, *Tinuspora Cordifolia, Curcuma xanthorrhiza* and *Averrhoa blimbi L*. were carried out by soaking the samples in 70% ethanol in a ratio of 1:10 for 24 hours while stirring for the first two hours. Remaceration was also carried out once so that the active substance in the *Simplicia* could be optimally extracted.

Preparation of the test animals

As shown in Figure 1, 42 white male rats (*Rattus norvegicus*) aged seven to eight weeks were used. They weighed 179.29 grams on average and were divided into seven groups (six in rats in each group). The groups included K1 = normal rats, K2 = hyperglycemic rats (induced by streptozotocin (STZ) + nicotinamide), K3 = hyperglycemic rats (induced by STZ + nicotinamide) + glibenclamide, K4 = hyperglycemic rats (induced by STZ + nicotinamide) + ethanolic Extract of *Tinuspora Cordifolia*, K5 = hyperglycemic rats (induced by STZ + nicotinamide) + ethanolic extract of *Averrhoa blimbi L*, K6 = hyperglycemic rats (induced by STZ + nicotinamide) + ethanolic extract of *Cinnamomum zeylanicum*, K7 = hyperglycemic rats (induced by STZ + nicotinamide) + *ethanolic* extract of Curcuma *xanthorrhiza*.

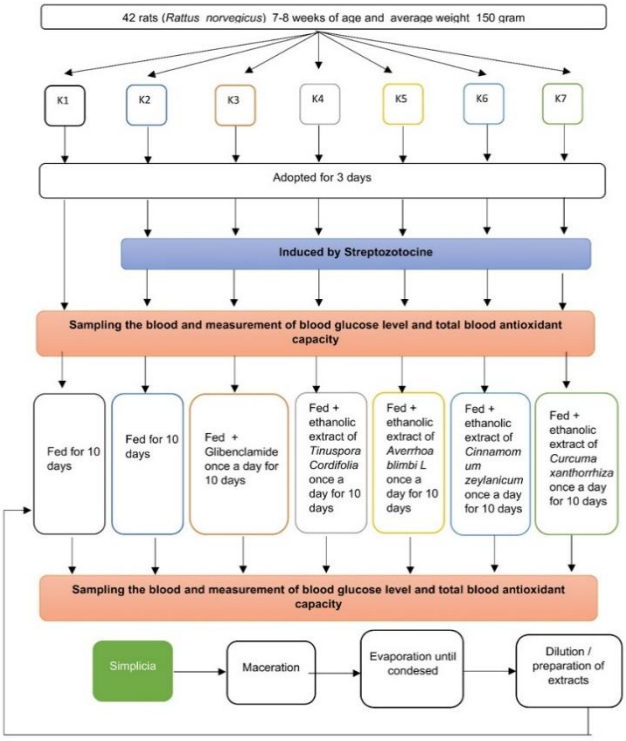


Figure 1: Experiment flow chart

Testing and experimental design

Firstly, all rats were conditioned to the laboratory conditions for three days. Then, the K2-K7 groups were given 45 mg of STZ per kg of body weight in order to make them hyperglycemic. Their blood glucose level was measured before and after STZ induction. Following this, the K3 group was given 0.09mg of glibenclamide per 200 g of body weight, K4 was given 90mg of ethanolic extract of *Tinuspora Cordifolia* per 200 g, K5 was given 15 mg of ethanolic extract of

Averrhoa blimbi L per 200 g of body weight, K6 was given 50 mg of ethanolic extract of *Cinnamomum zeylanicum* per 200 g of body weight, K7 was given 30 mg ethanolic extract of *Curcuma xanthorrhiza* orally per 200 g of body weight. At the end of the observation (day 11), the blood glucose level and total antioxidant capacity of plasma were measured.

Analysis

Reduction of the blood glucose level was calculated by subtracting the blood glucose level after ten days of the treatment from the blood glucose level before treatment. The same formula was also applied to measure the total antioxidant capacity of plasma. The mean differences of the blood glucose level and the total antioxidant capacity of plasma were analysed statistically using the One Way Anova test and LSD *post hoc* test with $\alpha = 0.05$ with SPSS statistic 25. The correlation between the total antioxidant capacity of plasma with the reduction of blood glucose level was analysed statistically by using regression in which reduction of blood glucose level acted as a dependent variable.

Result

Total antioxidant capacity of plasma before and after treatment

Figure 2 indicates that there was a significant difference between the mean antioxidant capacity of plasma between hyperglycemic rats that did not receive treatment and those that received ethanolic extract treatment. K1 and K2 were not treated with compounds that act as antioxidants. The antioxidant capacity improved in the group of rats that were treated with compounds for ten days, while the normal and hyperglycemic rats experienced a reduction (Figure 2). This meant that there was a decrease in free radical levels due to the ethanolic extract. The mean improvement of the total antioxidant capacity was different in the K3, K4, K5, and K6 groups, but the total antioxidant capacity value after treatment could be twice from the baseline (before treatment) or more, and it was observed to be statistically significant (p<0,05) using paired sample t-test pre and post-treatment (as shown in Table I). The comparative compound used was glibenclamide which is widely used to treat type 2 diabetes mellitus, and it was proved to successfully increase the antioxidant capacity of plasma. It indicated that the ethanolic extract of *Cinnamomum zeylanicum* was the strongest compound. It could increase the total antioxidant capacity of plasma better than *Tinuspora Cordifolia, Averrhoa blimbi L* or *Curcuma xanthorrhiza*.

The statistical analysis (Table I) revealed that the total antioxidant capacity of plasma between the K3 and K6 groups or between the K4 and K7 groups was not significantly different (p<0.05). This meant that the ethanolic extracts of *Cinnamomum zeylanicum* had the same antioxidant capacity as that of glibenclamide. Meanwhile, the ethanolic extracts of *Tinospora cordifolia* had the same antioxidant capacity as that of *Curcuma xanthorrhiza*.

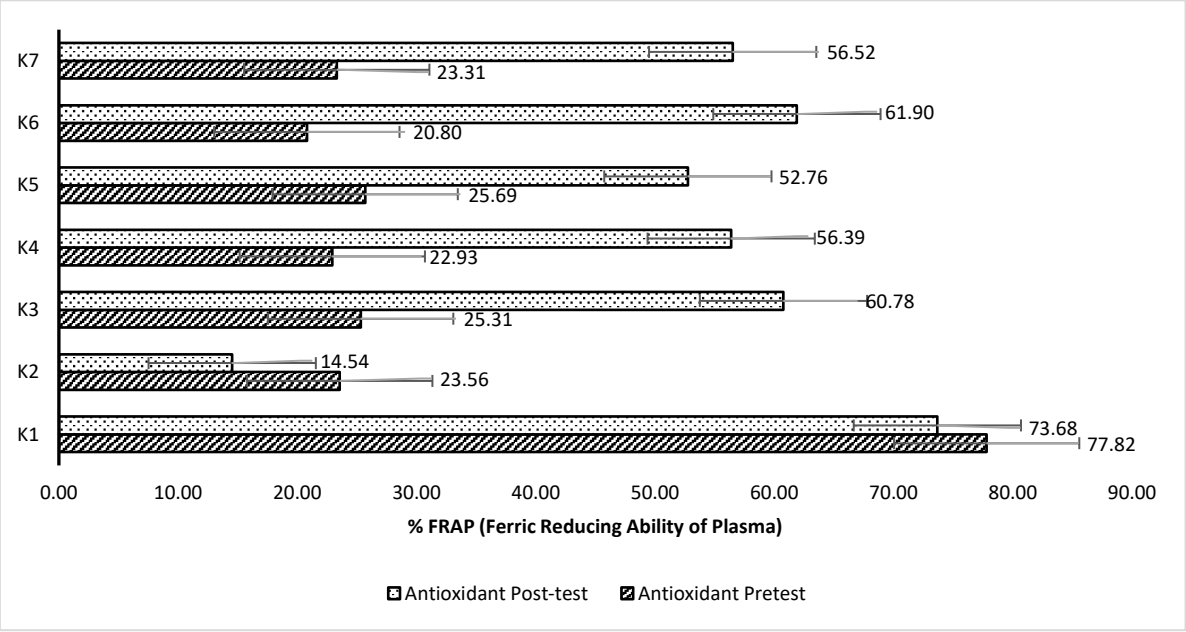


Figure 2: Total antioxidant capacity of plasma

Table I: Mean of the increase of the total antioxidant capacity of plasma and the reduction of blood glucose level

Group	Increase of the total antioxidant capacity of plasma (% FRAP)		Reduction of blood glucose level (mg/dL)	
	Mean	±SD	Mean	±SD
K1	-4.14	2.22	-2.91[a]	1.77
K2	-9.02	4.82	-4.56[a]	3.67
K3	40.10[a]	4.42	124.58[b]	7.05
K4	33.46[a]	2.46	117.68[c]	6.70
K5	27.07	3.52	108.68	7.69
K6	41.10	4.19	130.90[b]	3.43
K7	33.21[a]	2.91	123.01[c]	9.09

K1 = normal rats
K2 = Hyperglycemic rats (induced by STZ + nicotinamide)
K3 = Hyperglycemic rats (induced by STZ + nicotinamide) + Glibenclamide
K4 = Hyperglycemic rats (induced by STZ + nicotinamide) + Ethanolic Extract of *Tinuspora Cordifolia*
K5 = Hyperglycemic rats (induced by STZ + nicotinamide) + Ethanolic Extract of *Averrhoa blimbi L*
K6 = Hyperglycemic rats (induced by STZ + nicotinamide) + Ethanolic Extract of *Cinnamomum zeylanicum*
K7 = Hyperglycemic rats (induced by STZ + nicotinamide) + Ethanolic Extract of *Curcuma xanthorrhiza*
The same superscript letter showed that there were no differences between the groups (LSD *post hoc* ANOVA with *p-value* >0,05)

Blood glucose level before and after treatment

Figure 3 shows that the mean of the baseline blood glucose level (before STZ injection) in every group is placed on the same line. This means that the animals were healthy and homogenous, so they were able to be randomly separated into groups. After STZ injection, blood glucose levels in K2-K7 groups increased significantly and was placed at the same level. This meant that STZ successfully made the rats hyperglycemic and gave them type 2 Diabetes mellitus. Figure 3 also reveals that using ethanolic extract in treatment can decrease blood glucose levels significantly, although it has yet to be as effective as glibenclamide. It shows that ethanolic extract of *Cinnamomum zeylanicum* is the strongest compound at decreasing blood glucose levels compared to ethanolic extract of *Tinuspora Cordifolia, Averrhoa blimbi L* or *Curcuma xanthorrhiza*.

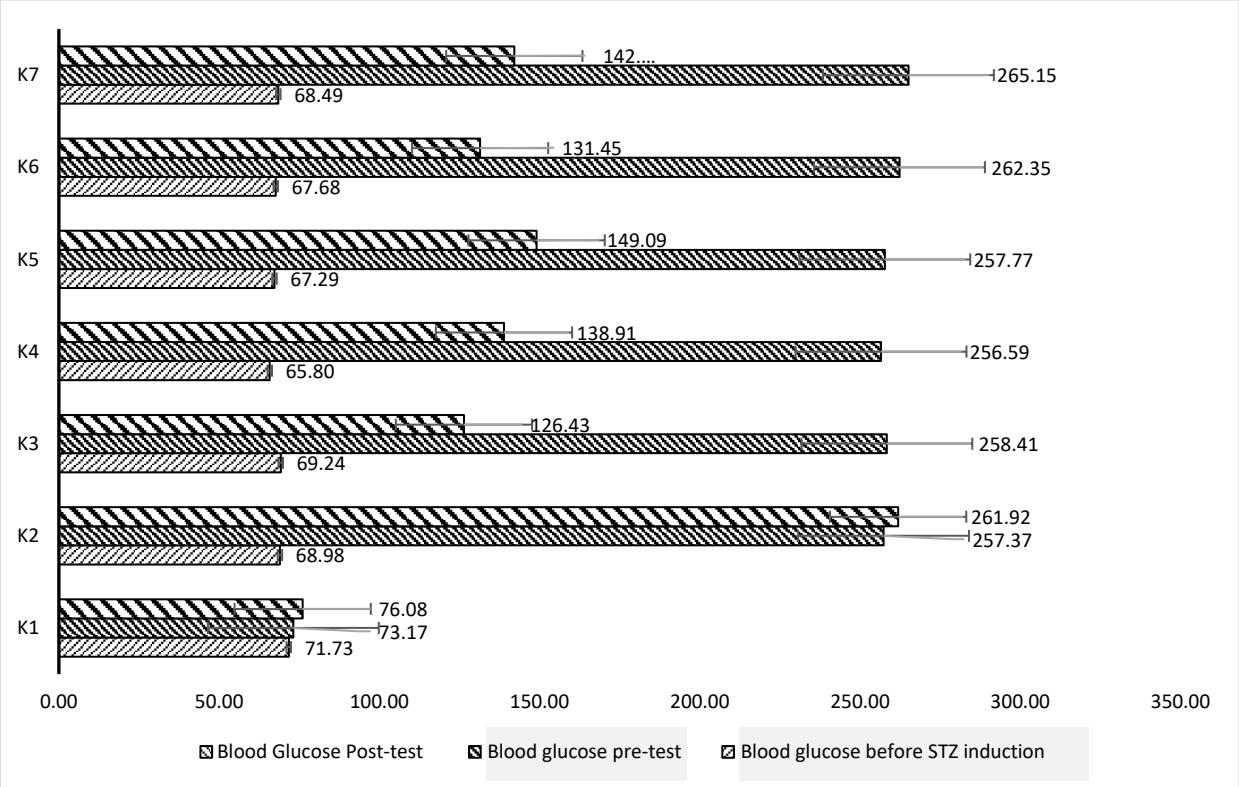
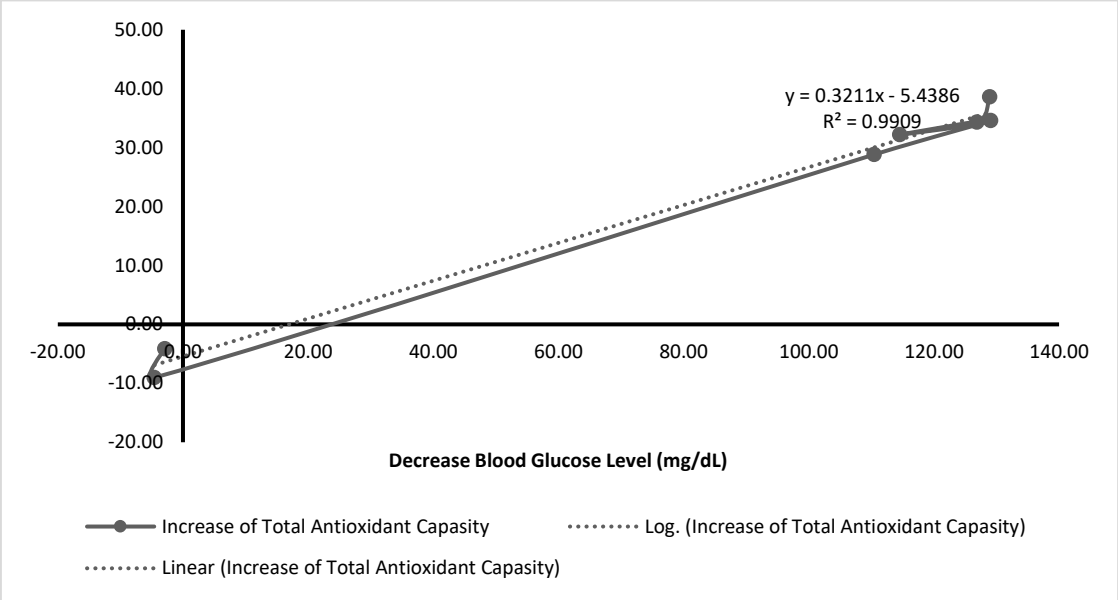


Figure 3: Blood glucose level before and after treatment

The correlation between the total antioxidant capacity of plasma and blood glucose level

The results of this study indicate that *Tinospora cordifolia* and *Curcuma zanthorrhiza* have equivalent potential to reduce blood glucose levels as glibenclamide, thereby increasing superoxide dismutase (SOD) activity and total antioxidant capacity in diabetic rats. This was approved by a linear relationship between the total antioxidant capacity of plasma and the glucose levels, which was inversely proportional to 96,67%. This states that there was a perfect negative linear relationship between the post-test mean of total antioxidant capacity variation and the mean of plasma glucose levels. The equation of this correlation, as shown in Figure 4, was y = 0,3211x – 5,4386. This means that for every 1mg/L of total antioxidant capacity of plasma (x) that is added, the glucose in the blood will decrease by 0.326 mg/dL.



Note: equation is y = 0.3211x – 5.4386 where y = blood glucose level, and x = antioxidant capacity of plasma

Figure 4: The correlation between total antioxidant capacity of plasma and blood glucose level

Discussion

Total antioxidant capacity of plasma was increased by treatment

Antioxidant potential was measured using the frap method. The principle of the frap method is based on the ability of the sample to transfer electrons to reduce the iron ion Fe^{3+} (ferro) to iron ion Fe^{2+} (ferri). Antioxidant capacity is one of the parameters that shows how much potential a substance has to act as an antioxidant (Pisoschi & Negulescu, 2012). The greater the total antioxidant capacity of plasma, the greater the ability of these compounds to act as antioxidants.

The total antioxidant capacity of the ethanolic extract from *Tinospora cordifolia*, *Cinnamomum zeylanicum*, and *Curcuma xanthorrhiza* is associated with the chemical compounds in these plants, which possess antioxidant activity. Polysaccharide compounds in the form of arabinogalactan, galacturonic acid, and neutral glucan found in *Cinnamomum zeylanicum* are known to act as antioxidants (Ghosh *et al*., 2015). *Cinnamomum zeylanicum* contains volatile oil with the main components being eugenol, cinnamaldehyde, and camphor which act as antioxidants, antimicrobials, and antidiabetic (Jayaprakasha & Rao, 2011). *Cinnamomum zeylanicum* bark and fruits contain proanthocyanidins which are flavonoids. In the ethanolic extract of *Tinospora cordifolia*, there are main components such as *tinocordioside*, *cordifolide* A, *palmatine*, *quercetin, β-sitosterol*, *heptacosanol*, and *syringin* (Kumar *et al*., 2018). One of the compounds that act as an antioxidant in *Tinospora cordifolia* is flavonoid quercetin. Quercetin is a 3-hydroxyl group flavonoid that neutralizes free radicals by one-step hydrogen atom or electron transfer followed by proton transfer during which they are oxidized (Lesjak *et al*., 2018). The essential oils contained in this plant are able to capture strong free radicals with DPPH with a total phenolic content of 28 ± 0.4 mg GAE / g (Naik *et al*., 2014).

The ability of free radical scavenging in *Curcuma xanthorhiza* is associated with chemical compounds contained in this plant, including curcumin, demethoxycurcumin, and bisdemethoxycurcumin, which have strong antioxidant activity (Jantan *et al.*,

2012). Curcumin is the compound with the strongest antioxidant ability compared to demetoxycurcumin and bisdemetethoxycurcumin (Jayaprakasha *et al.*, 2006).

Blood glucose level decreased by the treatment

Rats that were given STZ-induced DM had similar pathophysiology as type 2 DM patients. STZ 2-Deoxy-2-[[(methylnitrosoamino)carbonyl]amino]-D-glucopyranose is a cytotoxic glucose analogue, and its cytotoxicity is derived from the ßcell selective action mechanisms (Islam *et al*., 2017). STZ is selectively accumulated in pancreatic β cells via the low-affinity GLUT2 glucose transporter in the plasma membrane (Gauthier, 2014; Jayasimha Goud & Swamy, 2015). The effects of STZ on glucose and insulin homeostasis reflect the toxin-induced abnormalities in β cell function. Initially, insulin biosynthesis, glucose-induced insulin secretion and glucose metabolism (both glucose oxidation and oxygen consumption) are all affected (Nagarchi *et al.*, 2015; Wu & Yan, 2015). At later stages of functional β cell impairment, gene expression and protein production deficiencies lead to the deterioration of both glucose transport and metabolism (Khaki *et al*., 2014; Kumar M, 2017).

The results revealed that all of the extracts made blood glucose levels decrease, and the best performance was obtained when *Cinnamomum zeylanicum* extract was used. The mean reduction of blood glucose level gained by using ethanolic extract in *Cinnamomum zeylanicum* is statistically significantly similar to the mean reduction obtained by using glibenclamide. Other experts reported that cinnamon extract plays a role in regulating blood glucose levels and lipids. It may also exert a blood glucose-suppressing effect by improving insulin sensitivity or slowing the absorption of carbohydrates in the small intestine (Abd *et al.*, 2010; Sartorius *et al.*, 2014).

Phytochemical screening on cinnamon bark Simplicia indicates that the Simplicia contains secondary metabolite compounds, namely tannins, phenolics, flavonoids, quinones, saponins, monoterpenes, and sesquiterpenes (Adisakwattana *et al*., 2011; Assefa *et al*., 2018). Flavonoids stimulate glucose uptake in peripheral tissues, regulate the activity and/or express the rate-limiting enzymes in the carbohydrate metabolism canal, and act as insulin secretagogues or insulin mimetics, possibly influencing the pleiotropic mechanisms of insulin signalling to ameliorate the diabetes condition (Cazarolli *et al*., 2008; Testa *et al*., 2016).

There is a correlation between the escalation of total antioxidant capacity of plasma and the decline of blood glucose level

Diabetes mellitus is characterised by hyperglycemia and average haemoglobin A1c levels (HbA1c) above 48mmol/mol (6.5%) for two to three months (Jean-Marie, 2018). This is caused by vascular dysfunction due to repeated exposure and pathologically high d-glucose concentrations (Domingueti *et al.*, 2016). The occurrence of vascular dysfunction is caused by disruption of the nitric oxide (NO) canal and an increase in oxidative stress, which will cause changes in glucose metabolism (Ghasemi & Jeddi, 2017). The results show that the proactive phytochemical exploration of *Tinospora cordifolia* and *Curcuma zanthorrhiza* in this study was obtained by antioxidant compounds from the measurement of the total antioxidant capacity, which is important for reducing glucose in the blood in Streptozotocin-induced DM rats. If hyperglycemia is not controlled in a Diabetes mellitus patient, it will cause further oxidative stress because hyperglycemia in diabetes mellitus leads to the excessive production of free radicals. This is characterised by an increase in malondialdehyde (MDA), peroxidation index, and a decrease in antioxidant protection in the body (Domingueti *et al*., 2016; Fouelifack *et al*., 2019).

The content of antioxidant compounds is determined by the presence of free –OH (hydroxyl) functional groups and carbon-carbon double bonds, such as flavones, flavanones, squalene, tocopherol β-carotene and vitamin C (Babu *et al.*, 2013). These bioactive compounds support the linear relationship between the decrease in blood glucose and the total antioxidant capacity so that they can prevent further vascular dysfunction in Diabetes mellitus (Hussain *et al.*, 2020). The total antioxidant activity from the results of this study illustrates the antioxidant status of STZ-induced rat blood samples, and it proves that the antioxidant response to free radicals is produced due to hyperglycemic conditions. Antioxidant activity describes the ability of an antioxidant compound to neutralise free radicals so that it can delay, slow down, and prevent the occurrence of free radical anti-oxidation reactions in lipid oxidation (Shahidi & Zhong, 2015). The mechanism of reducing blood glucose levels is carried out by stimulating the secretion of the insulin hormone, increasing glucose uptake from blood to tissues, oxidating glucose, and activating glycogen synthesis in the liver and adipose tissue (Lee & Jun, 2014; Bhatt *et al.*, 2016). Increased cumulative action of all the antioxidants present in plasma and body fluids *in vivo* will be able to balance oxidants and antioxidants. As a result, oxidative stress will decrease, and this will be marked by a decrease in glucose in the

blood (Birben *et al.,* 2012; Jamuna Rani & Mythili, 2014; Pruchniak *et al*., 2016).

References

Abd, S. N., Rahman, E., Abdel-Haleem, A. M. H., & Al Mudhaffar, H. M. (2010). Antidiabetic effect of cinnAmon powder And cinnAmon Aqueous extrAct on serum glucose of rAts. *International Journal of Food, Nutrition and Public Health*.

Adisakwattana, S., Lerdsuwankij, O., Poputtachai, U., Minipun, A., & Suparpprom, C. (2011). Inhibitory Activity of Cinnamon Bark Species and their Combination Effect with Acarbose against Intestinal α-glucosidase and Pancreatic α-amylase. *Plant Foods for Human Nutrition*. https://doi.org/10.1007/s11130-011-0226-4

Alhassan, A., & Ahmed, Q. (2016). Averrhoa bilimbi Linn.: A review of its ethnomedicinal uses, phytochemistry, and pharmacology. In *Journal of Pharmacy and Bioallied Sciences*. https://doi.org/10.4103/0975-7406.199342

Annisa, F., Viryawan, C., & Santoso, F. (2014). Hipoksia Berpeluang Mencegah Kerusakan Sel β Pankreas pada Pasien Diabetes Melitus Tipe 2: Tinjauan Biologi Molekuler. *Cdk*

Assefa, A. D., Keum, Y. S., & Saini, R. K. (2018). A comprehensive study of polyphenols contents and antioxidant potential of 39 widely used spices and food condiments. *Journal of Food Measurement and Characterization*. https://doi.org/10.1007/s11694-018-9770-z

Babu, P. V. A., Liu, D., & Gilbert, E. R. (2013). Recent advances in understanding the antidiabetic actions of dietary flavonoids. In *Journal of Nutritional Biochemistry*. https://doi.org/10.1016/j.jnutbio.2013.06.003

Bhatt, H., Saklani, S., & Upadhayay, K. (2016). Antioxidant and antidiabetic activities of ethanolic extract of Primula Denticulata Flowers. *Indonesian Journal of Pharmacy*. https://doi.org/10.14499/indonesianjpharm27iss2pp74

Birben, E., Sahiner, U. M., Sackesen, C., Erzurum, S., & Kalayci, O. (2012). Oxidative stress and antioxidant defense. In *World Allergy Organization Journal*. https://doi.org/10.1097/WOX.0b013e3182439613

Cazarolli, L., Zanatta, L., Alberton, E., Reis Bonorino Figueiredo, M., Folador, P., Damazio, R., Pizzolatti, M., & Mena Barreto Silva, F. (2008). Flavonoids: Cellular and Molecular Mechanism of Action in Glucose Homeostasis. *Mini-Reviews in Medicinal Chemistry*. https://doi.org/10.2174/138955708785740580

Dewanjee, S., Das, S., Das, A. K., Bhattacharjee, N., Dihingia, A., Dua, T. K., Kalita, J., & Manna, P. (2018). Molecular mechanism of diabetic neuropathy and its pharmacotherapeutic targets. In *European Journal of Pharmacology*. https://doi.org/10.1016/j.ejphar.2018.06.034

Domingueti, C. P., Dusse, L. M. S. A., Carvalho, M. D. G., De Sousa, L. P., Gomes, K. B., & Fernandes, A. P. (2016). Diabetes mellitus: The linkage between oxidative stress, inflammation, hypercoagulability and vascular complications. In *Journal of Diabetes and its Complications*. https://doi.org/10.1016/j.jdiacomp.2015.12.018

Ervina, M., Nawu, Y. E., & Esar, S. Y. (2016). Comparison of in vitro antioxidant activity of infusion, extract and fractions of Indonesian Cinnamon (Cinnamomum burmannii) bark. *International Food Research Journal*

Fouelifack, F. Y., Sama, J. D., & Sone, C. E. (2019). Assessment of adherence to iron supplementation among pregnant women in the yaounde gynaeco-obstetric and paediatric hospital. *Pan African Medical Journal*. https://doi.org/10.11604/pamj.2019.34.211.16446

Gauthier, E. L. (2014). Streptozotocin: Uses, mechanism of action and side effects. In *Streptozotocin: Uses, Mechanism of Action and Side Effects*

Ghasemi, A., & Jeddi, S. (2017). Anti-obesity and antidiabetic effects of nitrate and nitrite. In *Nitric Oxide - Biology and Chemistry*. https://doi.org/10.1016/j.niox.2017.08.003

Ghorbani, A. (2017). Mechanisms of antidiabetic effects of flavonoid rutin. In *Biomedicine and Pharmacotherapy*. https://doi.org/10.1016/j.biopha.2017.10.001

Ghosh, T., Basu, A., Adhikari, D., Roy, D., & Pal, A. K. (2015). Antioxidant activity and structural features of Cinnamomum zeylanicum. *3 Biotech*, **5**(6), 939–947. https://doi.org/10.1007/s13205-015-0296-3

Hussain, T., Tan, B., Murtaza, G., Liu, G., Rahu, N., Saleem Kalhoro, M., Hussain Kalhoro, D., Adebowale, T. O., Usman Mazhar, M., Rehman, Z. ur, Martínez, Y., Akber Khan, S., & Yin, Y. (2020). Flavonoids and type 2 diabetes: Evidence of efficacy in clinical and animal studies and delivery strategies to enhance their therapeutic efficacy. In *Pharmacological Research*. https://doi.org/10.1016/j.phrs.2020.104629

Islam, M., Rupeshkumar, M., & Reddy, K. B. (2017). Streptozotocin is more convenient than Alloxan for the induction of Type 2 diabetes. *International Journal of Pharmacological Research*

Jamuna Rani, A., & Mythili, S. V. (2014). Study on total antioxidant status in relation to oxidative stress in type 2 diabetes mellitus. *Journal of Clinical and Diagnostic Research*. https://doi.org/10.7860/JCDR/2014/7603.4121

Jantan, I., Saputri, F. C., Qaisar, M. N., & Buang, F. (2012). Correlation between chemical composition of curcuma domestica and curcuma xanthorrhiza and their antioxidant effect on human low-density lipoprotein oxidation. *Evidence-Based Complementary and Alternative Medicine*, *2012*. https://doi.org/10.1155/2012/438356

Jayaprakasha, G. K., Ohnishi-Kameyama, M., Ono, H., Yoshida, M., & Rao, L. J. (2006). Phenolic constituents in the fruits of Cinnamomum zeylanicum and their antioxidant activity. *Journal of Agricultural and Food Chemistry*, **54**(5), 1672–1679. https://doi.org/10.1021/jf052736r

Jayaprakasha, G. K., & Rao, L. J. M. (2011). Chemistry, biogenesis, and biological activities of cinnamomum zeylanicum. *Critical Reviews in Food Science and Nutrition*, **51**(6), 547–562. https://doi.org/10.1080/10408391003699550

Jayasimha Goud, B., & swamy, Bkc. (2015). Streptozotocin -A Diabetogenic Agent in Animal Models www.ijppr.humanjournals.com. *Human Journals Review Article April*

Jean-Marie, E. (2018). Diagnosis and classification of diabetes mellitus. In *Encyclopedia of Endocrine Diseases*. https://doi.org/10.1016/B978-0-12-801238-3.65822-1

Khaki, A., Khaki, A. A., Hajhosseini, L., Golzar, F. S., & Ainehchi, N. (2014). The antioxidant effects of ginger and cinnamon on spermatogenesis dys-function of diabetes rats. *African*

Journal of Traditional, Complementary and Alternative Medicines. https://doi.org/10.4314/ajtcam.v11i4.1

Kim, M. B., Kim, C., Song, Y., & Hwang, J. K. (2014). Antihyperglycemic and anti-inflammatory effects of standardized Curcuma xanthorrhiza Roxb. Extract and its active compound xanthorrhizol in high-fat diet-induced obese mice. *Evidence-Based Complementary and Alternative Medicine*. https://doi.org/10.1155/2014/205915

Kumar M, S. (2017). Optimization of Yield for Extraction of an Essential Oil from Cinnamon Using Microwave-Assisted Extraction. *Journal of Chromatography & Separation Techniques*. https://doi.org/10.4172/2157-7064.s8-001

Kumar, V., Singh, S., Singh, A., Dixit, A. K., Srivastava, B., Sidhu, G. K., Singh, R., Meena, A. K., Singh, R. P., Subhose, V., & Prakash, O. (2018). Phytochemical, Antioxidant, Antimicrobial, and Protein Binding Qualities of Hydro-ethanolic Extract of Tinospora cordifolia. *Journal of Biologically Active Products from Nature*, **8**(3), 192–200. https://doi.org/10.1080/22311866.2018.1485513

Lee, Y. S., & Jun, H. S. (2014). Antidiabetic actions of glucagon-like peptide-1 on pancreatic beta-cells. In *Metabolism: Clinical and Experimental*. https://doi.org/10.1016/j.metabol.2013.09.010

Lesjak, M., Beara, I., Simin, N., Pintać, D., Majkić, T., Bekvalac, K., Orčić, D., & Mimica-Dukić, N. (2018). Antioxidant and anti-inflammatory activities of quercetin and its derivatives. *Journal of Functional Foods*, **40**, 68–75. https://doi.org/10.1016/j.jff.2017.10.047

Luo, Y., Peng, B., Wei, W., Tian, X., & Wu, Z. (2019). Antioxidant and antidiabetic activities of polysaccharides from guava leaves. *Molecules*. https://doi.org/10.3390/molecules24071343

Nagarchi, K., Ahmed, S., Sabus, A., & Saheb, S. H. (2015). Effect of Streptozotocin on glucose levels in albino wister rats. *Journal of Pharmaceutical Sciences and Research*

Naik, D., Dandge, C., & Rupanar, S. (2014). Determination of Chemical Composition and Evaluation of Antioxidant Activity of Essential Oil from Tinospora cordifolia (Willd.) Leaf. *Journal of Essential Oil-Bearing Plants*, **17**(2), 228–236. https://doi.org/10.1080/0972060X.2013.831568

Pisoschi, A. M., & Negulescu, G. P. (2012). Methods for Total Antioxidant Activity Determination: A Review. *Biochemistry & Analytical Biochemistry*. https://doi.org/10.4172/2161-1009.1000106

Pruchniak, M. P., Araźna, M., & Demkc, U. (2016). Biochemistry of oxidative stress. In *Advances in Experimental Medicine and Biology*. https://doi.org/10.1007/5584_2015_161

Puranik, N., Kammar, K. F., & Devi, S. (2010). Antidiabetic activity of tinospora cordifolia (Willd.) in streptozotocin diabetic rats; does it act like sulfonylureas? *Turkish Journal of Medical Sciences*. https://doi.org/10.3906/sag-0802-40

Sartorius, T., Peter, A., Schulz, N., Drescher, A., Bergheim, I., MacHann, J., Schick, F., Siegel-Axel, D., Schürmann, A., Weigert, C., Häring, H. U., & Hennige, A. M. (2014). Cinnamon extract improves insulin sensitivity in the brain and lowers liver fat in mouse models of obesity. *PLoS ONE*. https://doi.org/10.1371/journal.pone.0092358

Shahidi, F., & Zhong, Y. (2015). Measurement of antioxidant activity. In *Journal of Functional Foods*. https://doi.org/10.1016/j.jff.2015.01.047

Tangvarasittichai, S. (2015). Oxidative stress, insulin resistance, dyslipidemia and type 2 diabetes mellitus. *World Journal of Diabetes*. https://doi.org/10.4239/wjd.v6.i3.456

Testa, R., Bonfigli, A. R., Genovese, S., De Nigris, V., & Ceriello, A. (2016). The possible role of flavonoids in the prevention of diabetic complications. In *Nutrients*. https://doi.org/10.3390/nu8050310

Tiganis, T. (2011). Reactive oxygen species and insulin resistance: The good, the bad and the ugly. In *Trends in Pharmacological Sciences*. https://doi.org/10.1016/j.tips.2010.11.006

Wang, R., Wang, R., & Yang, B. (2009). Extraction of essential oils from five cinnamon leaves and identification of their volatile compound compositions. *Innovative Food Science and Emerging Technologies*. https://doi.org/10.1016/j.ifset.2008.12.002

Wu, J., & Yan, L. J. (2015). Streptozotocin-induced type 1 diabetes in rodents as a model for studying mitochondrial mechanisms of diabetic β cell glucotoxicity. In *Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy*. https://doi.org/10.2147/DMSO.S82272