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POTENTIAL OF ETHANOL EXTRACT OF GUAVA (PSIDIUM GUAJAVA L.) LEAVES AS ADJUVANT-ANTIBIOTIC ON SALMONELLA TYPHI CHARACTERIZED

Wahyu Hendrarti[*1], Muhammad Robiansyah[1], Syamsu Nur[2], Astuti Amin[2], Michrun nisa[3] and Hamdayani Lance Abidin[4]

[1]*Department Pharmacology and Clinical Pharmacy, Sekolah Tinggi Ilmu Farmasi Makassar, 90242, Makassar, Indonesia*
[2]*Depratment of Pharmaceutical Analysis and Medicinal Chemistry, Sekolah Tinggi Ilmu Farmasi Makassar, 90242, Makassar, Indonesia*
[3]*Depratment of Pharmaceutical Technology, Sekolah Tinggi Ilmu Farmasi Makassar, 90242, Makassar, Indonesia*
[4]*Depratment of Pharmaceutical Biology, Sekolah Tinggi Ilmu Farmasi Makassar, 90242, Makassar, Indonesia*

Guava (Psidium guajava L.) contains many chemical compounds, including quercetin, myricetin, epicatechin, and tannins which have been shown to have efficacy as an efflux pump inhibitor (EPI) in several pathogenic bacteria. This study aimed to investigate the synergistic effect of the ethanol extract of guava leaves with five common antibiotics on Salmonella typhi isolates expressing active efflux pumps. Bacterial characterization was carried out on clinical isolates of S. typhi, and molecular resistance mechanisms were determined using qRT-PCR by measuring the expression of the Acriflavine resistance protein B (AcrB) efflux pump. Guava leaves were extracted by maceration using 70% ethanol. Tests were carried out using the diffusion method with tetracycline, ampicillin, trimethoprim-sulfamethoxazole, chloramphenicol, and ciprofloxacin. The extract was made in serial concentrations of 0.01, 0.025, 0.05, 0.075, and 0.1%. The results showed that the tested isolates decreased the expression of AcrB from 11.48167 to 7.38818 ρg/mL after adding CCCP. The synergistic effect occurred at (1) extract concentration of 0.1% against tetracycline 30 µg, (2) concentration of 0.05% against ampicillin10µg, (3) concentration of 0.075% against trimethoprim-sulfamethoxazole 23.75-1.25 µg, (4) concentration of 0.05% against chloramphenicol 30 µg, (5) concentration of 0.025% against ciprofloxacin 5 µg. The ethanol extract of guava leaves (Psidium guajava L.) synergized with the studied antibiotics and displayed efflux pump inhibitory activity. Consequently, it could serve as a natural antibiotic adjuvant candidate.

Keywords: *Antibiotics, efflux pump inhibitor, guava leaves, Salmonella thypi ST019*

INTRODUCTION

Researchers said that in 2019 resistance to antimicrobials caused around 3.57 million deaths, and 1.27 million of them were caused by antibiotic resistance[1]. The World Health Organization (WHO) lists antimicrobial resistance as one of humanity's top 10 global public health threats[2]. It is the first to release a list of drug-resistant bacteria that pose the greatest threat to global health, including *Salmonella typhi (S. typhi*)[3]. This bacterium was reported in 2014 to have widespread resistance to the mainstay drug Fluoroquinolone[1], making it one of the causes of deadly diseases due to the scarcity of its antibiotics. Based on this, the discovery of new antibiotics is urgently needed[3]. The speed at which bacteria, especially gram-negative ones, develop antibiotic resistance far exceeds drug

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*Corresponding author: Wahyu Hendrarti, E-mail: wahyuhendrarti77@gmail.com

discovery, resulting in incurable infections. The search for adjuvant antibiotics is a promising alternative strategy to overcome this case[2,4].

Resistance in *S. typhi* and other organisms has been widely known, including bacteria-producing enzymes capable of degrading antibiotics such as β-lactamases, a permeability barrier played by the outer membrane, and intrinsic resistance due to overexpression of the antibiotic efflux pump[5]. The main mechanism of antibiotic resistance is due to the role of active efflux from bacteria which can cause failure to accumulate the amount of drug in bacterial cells. In this mechanism, antibiotics can enter the bacterial cell but are immediately pumped out of it actively outside of their normal work. This mechanism increases the frequency of failed therapy when using antibiotic drugs[6]. Genes encoding drug efflux pumps (protein-transporters) have been identified and isolated from several species of *S. typhi*. The efflux pump is a protein that transports typhoid drugs, including Chloramphenicol, Ampicillin, Trimethoprim-Sulfamethoxazole, tetracycline, and Ciprofloxacin. The AcrAB-Tolc efflux pump system is the most dominant transporter in *S. typhi*, especially AcrB, and can pump several types of drugs out of cells[7]. One strategy to overcome this problem is effective resistance modification through the search for efflux pump inhibitors (EPI) which can be combined with antibiotics and provide a synergistic effect or commonly called adjuvant antibiotics. Combining phytochemical agents with an antimicrobial will neutralize the resistance mechanism, allowing the drug to remain effective against resistant microbes[4].

Several synthetic EPIs, such as carbonyl cyanide m-chlorophenylhydrazone (CCCP) and phenyl–arginine-β-naphthylamide (PaβN), were found to be toxic to humans, so they were only used in in vitro studies[8,9]. Treat chlorpromazine, reserpine, verapamil, and omeprazole[8–11] in small concentrations can also function as an EPI. These drugs were also found to cause dangerous side effects, so the search for EPI from natural ingredients needs to be increased[12].

Natural adjuvants are used with antibiotics associated with high resistance levels, such as active efflux pumps. The synergism phenomenon, which reduces resistance (or increases sensitivity) even in multidrug-resistant bacteria, and several natural product compounds have been tested. Some of them are effective on various targets. Several compounds are active on almost all targets. For example, tellimagrandin and corilagin inhibit PBP2a (binding site of β-lactam antibiotics); gallic acid, thymol, and carvacrol increase the permeability of the bacterial outer membrane; epigallocatechin gallate (EGCG) inhibits β-lactamases; and reserpine, isopimarane, EGCG, and carnosic acid; and active substances found in the Apocynaceae family have been shown to inhibit bacterial efflux pumps[11,12].

Other studies have mentioned that several natural substances have efflux pump inhibition activity, including polyphenolics[13], such as quercetin, myricetin, epicatechin, and tannins[9,10,14]. These active substances can be obtained from *Psidium guajava* (L.), especially the leaves. *Psidium guajava* (L.) belongs to the Myrtaceae family and is an important fruit in tropical regions such as India, Indonesia, Pakistan, Bangladesh, and South America. Guava plant leaves have been studied for their health benefits. These are associated with the many phytochemical compounds or secondary metabolites they contain, such as flavonoids, triterpenoids, sesquiterpenes, glycosides, alkaloids, saponins, and other phenolic compounds. Specific compounds identified include quercetin, avicularin, apigenin, guaijaverin, kaempferol, hyperin, myricetin, gallic acid, catechins, epicatechin, chlorogenic acid, epigallocatechin gallate, tannins, and caffeic acid[15].

This study aims to determine the synergy effect and activity of efflux pump inhibitors of the ethanol extract of *Psidium guajava* (L.) guava leaves with several antibiotics on *S. typhi* isolates characterized as resistant due to active efflux pumps.

CHEMICALS AND METHODS

Chemicals

The chemicals use were ethanol (70 %w/w) Mueller-Hinton Agar (MHA), paper disk Chloramphenicol (30µg), Ampicillin (10µg), and Trimethoprim-Sulfametoxazole (1.25-23.75µg), tetracycline (30µg), and Ciprofloxacin (5µg)); Resistant *S. typhi* ST019

CCCP [Sigma], Primer gyrB gene, Acriflavine resistance protein B (AcrB), mix PCR, DMSO. The Guava leaf samples were obtained from Bajeng Village, Pattallassang District, Takalar Regency, South Sulawesi-Indonesia (5°24'43.2"S 119°25'59.1"E).

METHODS

Salmonella thypi Characterization

The test-bacterial screening was carried out on clinical isolates of *S. typhi* resistant to 1 or more antibiotics using CCCP (a synthetic efflux pump inhibitor used in the determination of the mechanism of resistance due to active efflux pump) treatment grown with 5 test antibiotics. After determining the sensitivity of each isolate, 1 loop was taken, and the resistance mechanism was determined molecularly using qRT-PCR (CFX connect system, Biorad Laboratories) with primers and PCR conditions according to the **Table 1** by measuring the expression of the efflux pump, namely AcrB, in isolates without and in the combination of 100µM CCCP.

Extract Preparation and Phytochemical Screening

Guava leaves were prepared by standard sorting and dried before being extracted by maceration using 70% ethanol. Evaporated with a rotary evaporator until a thick extract was obtained. The extract was subjected to a phytochemical screening in the form of a qualitative test of Flavonoids, Alkaloids, Saponins, and Tannins [16,17]. The extract was also carried out to ensure it was free from solvents with an ethanol-free test.

Efflux pump inhibition activity investigation

The method used was diffusion using MHA media and incubation at 37ºC for 24 hours, namely: Divided into 4 groups: (1) Group CCCP; (2) Group without extract and DMSO; (3) Group without DMSO combined extract; (4) Group Extracts of various concentrations. DMSO solvent was used to dissolve the extract. In each group, all the Petri dishes contained MHA media, *S. typhi* test isolates, and 5 different types of antibiotics. Group 1 added CCCP, group 2 did not add anything (contains only MHA media, *S. typhi*, and 5 types of test-antibiotics), group 3 only DMSO was added, and group 4 in each petri dish consisted of MHA, *S. typhi*, 5 types of antibiotics-test, 1 extract concentration. Each treatment was carried out in triplicate.

Data Analysis

Quantitative data in the form of the diameter of the antibiotic inhibition zone was analyzed descriptively based on the standard inhibition zone breakpoint according to CLSI (2021) and EUCAST (2021)[18,19].

RESULT AND DISCUSSION

In this study, the isolates of *S. typhi* bacteria were shown to have a resistance mechanism due to an active efflux pump. This was indicated by the decrease in the average value of AcrB efflux pump expression from 11.48 to 7.39 ρg/mL with the addition of CCCP **(Table 2)**. CCCP substance is a synthetic EPI that is often used in the characterization of resistance mechanisms in vitro. The EPI activity of CCCP is very strong and has a toxic effect on humans, so its use is limited for research[8,9]. This inhibitor was used in several previous studies to predict the resistance mechanism of an isolate or bacteria[20,21] or to study the role of the substance concerning the search for efflux pump inhibitors as an adjuvant antibiotic[9].

Table 1: Primer sequences of the AcrB gene and qRT-PCR conditions (19) (Baucheron, 2012).

Target gen	Primer	Oligonucleotide (5'–3') Sequences	Size (bp)	Annealing (°C)
acrB	acrB-f	TCGTGTTCCTGGTGATGTACCT	68	66
	acrB-r	AACCGCAATAGTCGGAATCAA		
gyrB	*gyrB-f*	TCTCCTCACAGACCAAAGATAAGCT	81	60
	gyrB-r	CGCTCAGCAGTTCGTTCATC		

Table 2: Characteristics of the test sample in the form of resistant *S. typhi* isolates mediated by active efflux.

Isolate code ST019	The average diameter of the zone of inhibition of antibiotics (mm) without and combination with CCCP									
	Chloramphenicol		Ampicillin		Trimetoprim-Sulfametoxazole		Tetracycline		Ciprofloxacin	
	A	B	A	B	A	B	A	B	A	B
	8.9 ±0.43	19.4 ±0.77	8.7 ±0.46	23.1 ±1.9	8.2 ±0.67	17.8 ±0.57	13.9 ±0.10	23.2 ±0.53	30.7 ±0.6	32.3 ±1.23
Sensitivity category*	R	S	R	S	R	S	I	S	S	S
Expression of AcrB (ρg/mL)	A					B				
	11.48					7.39				

Notes: A = without the addition of CCCP; B=CCCP combination; S=Sensitive; I=Intermediate; R=Resistance; Chloramphenicol; (S=≥18mm; I=13-17mm; R=≤12mm); Ampicillin (S=≥17mm; I=14-16mm; R=≤13mm); Trimethoprim-Sulfamethoxazole (S=≥16mm; I=11-15mm; R=≤11mm); Tetracycline (S ≥ 15mm; I = 12-14mm, ≤ 11mm); Ciprofloxacin (S ≥ 31mm; I = 21-30mm; R≤ 20mm)[18,19].

The group of *S. typhi* isolates before and after the addition of CCCP was tested molecularly by looking at the expression of its AcrB efflux pump. AcrB Efflux Pumps is a member of the resistance-nodulation-cell division (RND) superfamily. Overexpression of this efflux pump contributes to increased antibiotic resistance, especially in gram-negative bacteria[22]. The suppression of AcrB expression in the group combined with EPI (CCCP) indicated that the *S. typhi* bacteria used in the study had an active efflux pump resistance mechanism. Furthermore, this *S. typhi* isolate was used to test EPI activity from natural ingredients, namely guava leaves.

Guava leaves were extracted with 70% ethanol, and the results of phytochemical screening showed that this plant contains flavonoids, tannins, and saponins **(Table 3)**. According to Kumar et al.[15], guava leaves contain flavonoid compounds including quercetin, avicularin, apigenin, guaijaverin, kaempferol, hyperin, myricetin, and phenolic compounds including gallic acid, catechins, epicatechins, chlorogenic acid, epigallocatechin gallate, caffeic acid and also tannin compounds[18]. These compounds have activity as EPI[9,10,14]. Although only qualitative tests were carried out with compound classes in this study, this has provided an initial picture of the active compound content, which is strongly suspected of having EPI properties.

Table 3: Phytochemical screening analysis of extract.

Group compounds	Identification results
Flavonoid	+
Tannin	+
Alkaloid	-
Saponin	+

Notes: (+) positive results, (-) absence in guava leaves extract.

Tests in determining the EPI activity of guava leaf extract obtained the results of the initial sensitivity test on *S. typhi* showing that the group that was not added to the extract was resistant to chloramphenicol, ampicillin, and trimethoprim-sulfamethoxazole; Intermediate category or has decreased sensitivity to tetracycline; and still sensitive category to ciprofloxacin **(Table 5 and 6)**. The activity of the efflux pump inhibitor (EPI) of the ethanol extract of guava leaves was determined by first measuring the diameter of the antibacterial-test inhibition zone (chloramphenicol (30µg), ampicillin (10µg), trimethoprim-sulfametoxazole (1.25-23.75µg), tetracycline (30µg)), and ciprofloxacin (5µg), then compared between the group without extract and the group with the combination of extracts. Suppose there is an increase in the diameter of the inhibition zone and an increase in the sensitivity category of the antibacterial test from Resistant or Intermediate. In that case, it becomes sensitive again after adding the extract. Sensitivity category, intermediate, and resistance from the test results were observed and adjusted to the standard breakpoint diameter of the inhibition zone from EUCAST, 2021, and CLSI, 2011[18,19] **(Table 4).**

The test antibiotics used in this study are classic drugs in treating typhoid infection due to *S. typhi*. Ciprofloxacin is a fluoroquinolone group initially used to treat resistance to classic drugs but later also experienced a widespread acceleration of resistance. In 2014, it was reported that *S. typhi* bacteria had widespread resistance to the mainstay drug fluoroquinolone [1], making it one of the causes of deadly diseases due to the scarcity of antibiotics. *S. typhi* isolates in this study were found to be still sensitive to ciprofloxacin. This is possible because the prevalence of resistance was still less than the other 4 classic drugs. Ciprofloxacin is still included as one of the antibiotic tests intended to see EPI activity against drugs that are not yet resistant so that there can be an initial description of the mechanism of extract acts as an antibiotic adjuvant candidate.

Table 4: The standard breakpoint diameter (mm) of the inhibition zone.

No	Antimicrobial	Concentration (µg)	Diameter (mm)		
			S	I	R
1	Trimetoprim-Sulfametoxazole	23.75-1.25	≥16	11-15	≤11
2	Ampicillin	10	≥17	14-16	≤13
3	Chloramphenicol	30	≥18	13-17	≤12
4	Tetracycline	30	≥ 15	12-14	≤ 11
5	Ciprofloxacin	5	≥ 31	21-30	≤20

Notes: (S) sensitive, (I) intermediate, and (R) resistant.

Table 5: The Inhibition zone diameter (mm) of several antibiotics.

Inhibition zone diameter (mm) of antibiotics:								
Antibiotics	CCCP	No extract	No extract	Guava leaf extract in concentration (%) of:				
		(-DMSO)	(+DMSO)	0.01	0.025	0.05	0.075	0.1
Tetracycline	23.2 ±0.53	13.9 ±0.10	13.9 ± 0.23	14.4 ±2.27	16 ±0.53	16.9 ±0.67	17.5 ±1.86	21.1 ±2.50
Ampicillin	23.1 ±1.9	8.7 ±0.46	9.1 ±0.4	6.6 ±0.00	13.3 ±0.97	19.3 ±0.73	10.5 ±0.36	10.2 ±0.47
Trimetoprim-Sulfametoxazole	17.8 ±0.57	8.2 ±0.67	8.4 ±0.67	7.2 ±1.04	10.7 ±0.95	11.1 ±0.64	16.4 ±0.53	8.2 ±1.47
Chloramphenicol	19.4 ±0.77	8.9 ±0.43	9.1 ±0.46	8.7 ±0.95	10.5 ±0.38	14.3 ±0.76	11.7 ±1.08`	9.4 ±0.85
Ciprofloxacin	32.3 ±1.23	30.7 ±0.6	33.2 ±1.13	33 ±0.3	33.8 ±0.3	33.5 ±1.23	32.2 ±0.83	33.4 ±0.2

Notes: (-DMSO) is the means without DMSO, (+DMSO) is the means with DMSO as solvent. In this study, we compared sample extracts dissolved with DMSO and without DMSO to observe the inhibitory effect and sensitivity of DMSO solvent on each antibiotic. Tests were carried out without the addition of DMSO, namely when the initial screening was determined whether the *S. typhi* used was in the sensitive, intermediate, or resistance zone based on the inhibition zone.

Table 6: The sensitivity category of antibiotics.

Sensitivity category of antibiotics:								
Antibiotics	CCCP	No extract	No extract	With extract (%)				
		(-DMSO)	(+DMSO)	0,01	0,025	0,05	0,075	0,1
Tetracycline	S	I	I	I	**S**	**S**	**S**	**S**
Ampicillin	S	R	R	R	I	**S**	R	R
Trimetoprim-Sulfametoxazole	S	R	R	R	R	R	**S**	R
Chloramphenicol	I	R	R	R	R	I	R	R
Ciprofloxacin	S	S	S	S	S	S	S	S

Notes: S=Sensitive; Intermediate=Resistant; Chloramphenicol; (S=≥18; I=13-17; R=≤12) *based on CLSI, (2011) and Eucast, (2022).

S. typhi experienced increased sensitivity or susceptibility to antibiotics in the test after adding guava leaf extract at 1 or several concentrations. This provides information that the amount or ratio of ethanol extract from guava leaves (*Psidium guajava* L.) can affect EPI activity. The CCCP group was the positive control group, and in testing *S. typhi* bacteria with 30 µg tetracycline antibiotics, the average inhibition zone was 23.2 ± 0.53 sensitive category (S). This indicates that in the presence of CCCP, the *S. typhi* test bacteria with tetracycline antibiotics, which initially had an inhibition zone of 13.9 ± 0.10 mm in the intermediate (I) category, experienced an increase in the inhibition zone and became sensitive again. In testing with guava leaf extract, there was also an increase in the inhibition zone and a change in category at each extract concentration starting from 0.025, 0.05, 0.075, and 0.1% **(Table 5)**. The synergism effect occurred with an increase in the inhibition zone of the test antibiotics and a change in the category to become sensitive again. The highest concentration provides a synergistic effect between tetracycline and guava leaf extract at 0.1%.

The CCCP group on the *S. typhi* bacterial test with the antibiotic ampicillin 10µg obtained an average inhibition zone of 23.1 ± 1.9 mm in the sensitive category (S). This indicates that in the presence of CCCP, the *S. typhi* test bacteria with the antibiotic ampicillin which initially had an inhibition zone of 8.7 ± 0.46 mm in the resistant category (R), experienced an increase in the inhibition zone and became sensitive again. In testing with guava leaf extract, there was also an increase in the inhibition zone and a change in the category to be sensitive again at an extract concentration of 0.05% **(Table 6)**. The synergism effect occurs with an increase in the inhibition zone and a change in this category. The highest concentration provides a synergistic effect between ampicillin and guava leaf extract at 0.05%.

The CCCP group on the *S. typhi* bacteria test with trimethoprim-sulfametoxazole 23.75-1.25 µg obtained an average inhibition zone of 17.8 ± 0.57 sensitive category (S). This indicates that in the presence of CCCP, the test bacteria *S. typhi* with the antibacterial trimethoprim-sulfamethoxazole, which initially had an inhibition zone of 8.2 ± 0.67 mm in the resistance (R) category, experienced an increase in the inhibition zone and became sensitive again. In testing with guava leaf extract, there was also an increase in the inhibition zone and a change in category at an extract concentration of 0.075% **(table 6).** The synergism effect occurs with an increase in the inhibition zone and a change in these categories. The highest concentration gave a synergistic effect between trimethoprim-sulfamethoxazole and guava leaf extract, namely at 0.075%. In trimethoprim-sulfamethoxazole antibiotics, the activity of bacterial efflux pumps as a cause of resistance is less influential than other resistance mechanisms[23], but recently this resistance

mechanism has been widely found, including in *Stenotrophomonas maltophilia* bacteria so that this assumption is slightly contradictory[24]. The active efflux pump is an intrinsic resistance mechanism that can deactivate almost all antibacterials or antibiotics in almost all types of bacteria[9].

The CCCP group on the *S. typhi* bacteria test with 30 μg chloramphenicol antibiotic obtained an average inhibition zone of 19.4 ± 0.77 in the intermediate category (I). This indicates that in the presence of CCCP, the *S. typhi* test bacteria with the antibiotic chloramphenicol initially had an inhibition zone of 8.9 ± 0.43 mm, and the resistance (R) category experienced an increase in the inhibition zone, but the category only reached intermediate. In testing with guava leaf extract, there was also an increase in the inhibition zone and a change in category at an extract concentration of 0.05% **(Table 5).** The synergism effect occurs with an increase in the inhibition zone of the test antibiotics and a change in category. The highest concentration provides a synergistic effect between chloramphenicol and guava leaf extract at 0.05%.

The CCCP group on the *S. typhi* bacteria test with 5 μg ciprofloxacin antibiotic obtained an average inhibition zone of 32.3 ± 1.23 in the sensitive category (S). This indicates that in the presence of CCCP, the test bacteria *S. typhi* with the antibiotic ciprofloxacin initially had an inhibition zone of 30.7 ± 0.6 mm, the category was still sensitive (S) experienced an increase in the inhibition zone, and the category remained sensitive (S). In testing with guava leaf extract, there was also an increase in the inhibition zone at all tested extract concentrations, namely 0.01, 0.025, 0.05, 0.075, and 0.1%. The synergism effect occurs with an increase in the inhibition zone of the test antibiotics. The highest concentration provides a synergistic effect between ciprofloxacin and guava leaf extract at 0.025% **(Table 6)**. In testing the extract against the ciprofloxacin antibiotic, it was still carried out even though the *S. typhi* bacteria showed a sensitive category effect to know the synergistic effect of adding the extract.

Overall, it can be seen that the ethanol extract of guava leaves (*Psidium guajava* L.) shows potential as an efflux pump inhibitor (EPI) because after being grown with the test antibiotics, there is an increase in strength (sensitivity). This can be seen from a change in the sensitivity category for tetracycline, ampicillin, and trimethoprim-sulfamethoxazole, which were originally resistant to become sensitive again. There is a weak activity in the combination between the extract and Chloramphenicol where the originally resistant antibiotic turns into an Intermediate, and the antibiotic adjuvant added to Ciprofloxacin which was in the non-resistant category, turned out to have no effect.

Each test on each group of extracts shows that the extract has the effect of increasing the antibiotic inhibition zone, which was originally small or was in the resistant category to become sensitive again. The synergism effect occurs at (1) extract concentration of 0.1% against Tetracycline antibiotic 30 μg, (2) concentration of 0.05% against ampicillin 10 μg, (3) concentration of 0.075% against trimethoprim-sulfametoxazole 23.75-1.25 μg, (4) concentration of 0.05 % to chloramphenicol 30 μg, (5) concentration 0.025% to ciprofloxacin 5 μg. Extract concentrations that provide synergistic effects appear to be different for different antibiotics. This still needs to be studied in more depth. Efflux pump inhibitors act by various mechanisms, including competition between the pump protein substrate and the antibiotic at the binding point.

EPI potential in this extract is suspected from the active substances of the flavonoid types quercetin, myricetin, epicatechin, and tannin compounds. These compounds have been proven in research by[9] as EPI from natural ingredients even though the active substance was extracted from different plants and tested with other bacteria. The mechanism of action of EPI is thought to include (1) changing the molecular structure of the efflux pump so that its affinity for the drug decreases, (2) suppressing the expression of the efflux pump gene, (3) reducing the energy of the efflux pump (4) or being a competitive or non-competitive substrate for the efflux pump[11,25].

Conclusion

Experimentally, ethanol extract with a concentration of 0.05% increased the sensitivity of the antibiotics tetracycline, ampicillin, and ciprofloxacin with the sensitive

category and chloramphenicol with the intermediate category. At the same time, the sensitivity of the antibiotic trimethoprim-sulfamethoxazole requires an effective concentration of 0.075% to be in the sensitive category. This study illustrates that the ethanol extract of guava leaves (Psidium guajava L.) can synergize to increase antibiotic sensitivity which is thought to be an efflux pump inhibitor so that in the future, it can be further developed as a natural antibiotic adjuvant candidate.

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نشرة العلوم الصيدلية
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امكانية فعالية مستخلص الإيثانول لأوراق الجوافة (بسيديم جوافة ل.) كمضاد حيوي مساعد على مرض السالمونيلا التيفية

واهيو هندرارتي[1*] – محمد روبيانسياه[1] – سيامسو نور[2] – أستوتي أمين[2] – مشرون نيسا[3] – همداياني لانس عابدين[4]

[1] قسم الصيدلة والصيدلة السريرية، سيكولاه تينجي إيلمو فارماسي ماكاسار، ٩٠٢٤٢، ماكاسار ، إندونيسيا

[2] قسم التحليل الصيدلي والكيمياء الطبية ، سيكولاه تينجي إيلمو فارماسي ماكاسار، ٩٠٢٤٢ ، ماكاسار ، إندونيسيا

[3] قسم التكنولوجيا الصيدلانية، سيكولاه تينجي إيلمو فارماسي ماكاسار ، ٩٠٢٤٢ ، ماكاسار ، إندونيسيا

[4] قسم البيولوجيا الصيدلانية، سيكولاه تينجي إيلمو فارماسي ماكاسار ، ٩٠٢٤٢، ماكاسار ، إندونيسيا

تحتوي الجوافة (بسيديم جوافة ل.) على العديد من المركبات الكيميائية، بما في ذلك كيرسيتين، ميريسيتين، إيبيكاتشين، والعفص والتي ثبت أن لها فعالية كمثبط لمضخة التدفق في العديد من البكتيريا المسببة للأمراض. هدفت هذه الدراسة إلى معرفة التأثير التآزري لمستخلص الإيثانول من أوراق الجوافة مع خمسة مضادات حيوية شائعة على عزلات السالمونيلا التيفية المعبرة عن مضخات التدفق النشطة. تم إجراء التوصيف البكتيري على العزلات السريرية لسالمونيلا تيفي ، وتم تحديد آليات المقاومة الجزيئية باستخدام تفاعل البوليميراز المتسلسل اللحظي الكمي عن طريق قياس التعبير عن مضخة تدفق بروتين مقاومة الأكريفلافين. تم استخلاص أوراق الجوافة عن طريق النقع باستخدام ٧٠% الإيثانول. تم إجراء الاختبارات باستخدام طريقة الانتشار مع التتراسيكلين والأمبيسلين وتريميثوبريم–سلفاميثوكسازول والكلورامفينيكول والسيبروفلوكساسين. تم عمل المستخلص بتركيزات متسلسلة ٠,٠١، ٠,٠٢٥، ٠,٠٥، ٠,٠٧٥، و٠,١%. أظهرت النتائج أن العزلات المختبرة قللت من تعبير مضخة تدفق بروتين مقاومة الأكريفلافين من ١١,٤٨١٦٧ إلى ٧,٣٨٨١٨ بيكو جرام \ ملي بعد إضافة CCCP. حدث التأثير التآزري عند (١) تركيز المستخلص ٠,١% ضد التتراسيكلين ٣٠ ميكروجرام، (٢) تركيز ٠,٠٥% ضد أمبيسلين ١٠ ميكروجرام، (٣) تركيز ٠,٠٧٥% ضد تريميثوبريم– سلفاميثوكسازول ٢٣,٧٥–١,٢٥ ميكروجرام، (٤) تركيز ٠,٠٥ % ضد كلورامفينيكول ٣٠ ميكروجرام، (٥) تركيز ٠,٠٢٥% ضد سيبروفلوكساسين ٥ ميكروجرام. تم دمج مستخلص الإيثانول من أوراق الجوافة (بسيديم جوافة ل.) مع المضادات الحيوية المدروسة وأظهر نشاطًا مثبطًا لمضخة التدفق. وبالتالي، فإنه يمكن أن يكون بمثابة مرشح مساعد المضادات الحيوية الطبيعية.