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Review study on antibacterial activity of cherry leaf (*Muntingia calabura*) against *Staphylococcus spp.* and *Salmonella spp.* the most causing disease in livestock

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ABSTRACT: This research was conducted to know the potential activity of cherry leaf (*Muntingia calabura*) as an alternative medicine for diseases caused by the bacteria *Staphylococcus spp.* and *Salmonella spp.* The material of this study used some literature which relates to the paper's topic. The descriptive method was used to explain and describe the findings in the discussion chapter. A study of the effectiveness of the cherry leaf (*Muntingia calabura*) was made with other natural antibacterial sources such as sirih leaf (*Piper betle L.*) and beluntas leaf (*Pluchea indica L.).* The result of this study showed that cherry leaf extract was an effective natural antibacterial source because it had the widest inhibited zone against *Staphylococcus spp.* and *Salmonella spp.* which amounted to (19 mm and 37.7 mm respectively) as compared to beluntas leaf (9.5 mm and 15.9 mm respectively) and sirih leaf (16 mm and 17 mm respectively). The other significant result showed that *Muntingia calabura* was effective for duck egg hatchability which amounted to 87.74%. This result was higher than chemical antibacterial (80.81%), beluntas leaf (44.05%) and sirih leaf (46.43%). From all the literature reviewed about widest inhibited zone of natural antibacterial activity such as cherry leaf, beluntas leaf and sirih leaf against *Salmonella spp.* and *Staphylococcus sp,* the same extraction treatment was used. The result from the duck egg hatchery experiment between chemical antibacterial and natural antibacterial showed that they have the same treatment and effect on duck egg incubation time. It is suggested that further research is conducted to find out if the cherry leaf can be used as an alternative natural antibacterial for diseases caused by other bacteria.

Keywords*: antibacterial, chemical, natural, cherry leaf, bacteria*

INTRODUCTION

Food consumption is increasing each passing year rapidly due to increasing world population. Badan Pusat Statistik (2015) reported that most of the animal product consumption increase happened in 2014 and 2015. Although the demand for animal products is on the rise, this country still has a low level of consumption compared with other nations. As explained by Chandra (2016), one good example is Indonesia in 2016 where beef meat consumption was only at 2.61 kg/GDP,a meager amount compared with Argentina which consumed 55 kg/GDP. The existing imbalance between supply and demand of animal products has a significant effect on the consumption rate of the Indonesian people. This implies that this country must increase the livestock population to increase the GDP (Gross Domestic Product) in the livestock sector.

There are two types of factors that have been affecting livestock conditions; external and internal. As Johnson et al., (2016) has found out, external factors that can affect animal production are farm size and technology adaptation on the farm whereas internal elements can be disease handling techniques and genetic composition.

According to Budiharta and Warudju (1985), *Staphylococcus aureus* causes mastitis (a livestock disease in dairy cows), and farmers apply chemical antibacterial to heal that disease. In 2015, Kementrian Kesehatan Republik Indonesia (Ministry of Health Indonesia) suggested that *Staphylococcus aureus* should be included in the category of multi-resistance bacteria. The WHO also reported in 2016 that there were 480.000 new cases of multidrug resistance in the world. This means that antimicrobial resistance is a serious problem. Kemal (2014) reported the effect of *Salmonella spp.* infection as being dangerous. Some of the targets of the bacteria are in the digestive tract and reproductive tract. This makes the animals sick and decreases the farmer's income. For example, *Salmonella typhimurium* causes abortion in cattle, sheep, and horses. This means that bacteria interrupts the replacement cycle of livestock on a farm and with this, the farmer cannot fulfil the consumers' needs (as there is an imbalance between demand and what the farmer can supply). Besides the effect on the internal composition of affected livestock, the bacteria can be spread by the air to affect other animals.

Based on this explanation, there is the need for a natural better to substitute the chemical antibacterial. One of the potential tropical plants which can be used as a natural antibacterial is the cherry leaf *(Muntingia calabura)*. The major benefit of the natural anti-bacteria is that it does not show significant side effects on the test subject. This review study intends to assist the farmer with one of the best natural antibacterials that can be used to increase livestock productivity which will in turn automatically raise the farmer's income.

RESULTS AND DISCUSSION

Livestock farming in Indonesia

The development of livestock farming in Indonesia has been increasing every year. The farm products commonly consumed by Indonesian people come mainly from cattle, poultry, swine, and ducks. Nevertheless, according to Direktorat Jenderal Peternakan dan Kesehatan Hewan (2016) livestock population increased in previous years but not significantly. For example, the broiler population in 2015 was 1,528,329 heads, and this number rose to 1,592,669 heads in 2016. There was an increase of only 64,360 heads in one year equivalent to 4.21%. Factors that affect livestock population can be grouped into 'external' and 'internal'. External factors that affect livestock population include weather, diseases, and parasites which all influence livestock productivity. Internal factors include adaptation, nutritional practices, disease handling and adaptation to diet.

Indonesia is located in South East Asia and having tropical weather, many diseases affecting livestock health and productivity occur in the country. Common diseases which attack livestock are endemic to the tropics. Endemic parasites which cause the diseases are a major source of economic loss in animal husbandry and especially in tropical areas and developing countries, but as will be discussed later, the extent of those losses is yet to be accurately specified. Knowledge about the economics of treatment of these diseases is inadequate mostly because the farmer's financial restraints and that the results of treatment are not well known (Tisdell et.al., 1999).

The response functions should be weighed in relation to economic variables of importance (e.g. depending on the situation, weight gain, reproduction rates, lactation of mammalian livestock), rather than just clinical effects. Cooperation between veterinarians and economists is needed at an early stage if information of economic relevance is to be collected by veterinarians. The case in Indonesia is that majority of the bacterial livestock diseases are caused by *Staphylococcus spp.* and *Salmonella spp.*

Chemical antibacterials

Many people have been using synthetic antibacterials to kill bacteria which is a fast and easy way. This is usually mixed with livestock feed. The kind of chemical antibacterial commonly used is an antibiotic. Antibiotics include naturally occurring, semi-synthetic and synthetic chemical compounds which promote antimicrobial activity. They are used in veterinary medicine to treat and prevent disease, and for other purposes including growth promotion in livestock. Antibiotics can be administered orally, parenteral or topical. Antibiotics are commonly administered to livestock in the USA and Australia via feed, water or slow release implant (Khan et al., 2007).

The use of antibiotics sometimes results to residues in meat, milk, and eggs. Murdiati (1997) reported microbes were resistant to drugs like penicillin for healing infections and remedying allergies for around 10% of the global human population. The residue inside the livestock's body could be prevented by proper a antibiotic withdrawal time. This period was established to safeguard people from exposure to antibiotic-contaminated food. The withdrawal time is the time required for the residue of toxicological concern to reach safe concentration as defined by tolerance. In reality, many farmers ignore the withdrawal time because they want maximum income from their efforts. Based on this explanation, there is a need for an alternative for the chemical antibacterials. One alternative is the natural antibacterial which is safer for livestock, humans and the environment.

Natural antibacterials

Some researchers have found the solution for treating diseases caused by *Staphylococcus spp.* and *Streptococcus spp by* using natural antibacterials. Natural antibacterials can be found in Indonesia's local flora. The plants have many active compounds including flavonoids, tannin, saponins, sterol, alkaloids, and glycosides which can be used to inhibit the bacteria itself. Many of the research works have used the ethanol extraction method to obtain the maximum amount of the chemical compound inside the leaf. The comparison of the active compounds between (*Muntingia calabura*), sirih leaf (*Piper betle Linn)*, beluntas leaf (*Pluchea indica L.*) by use of the ethanol extract method is presented in Table 1.

Table 1. Comparison of active compound from each natural antibacterial plant

Extract (leaves)	Constituents						
	Flavonoid	Tanin	Saponins	Sterols	Triterpenes	Alkaloids	Glycosides
Cherry [a]	+++	++	+++	+	-	+	++
Sirih[b]	+	+	-	+	-	+	-
Beluntas[c]	++++	++	+	+++	-	++++	++

+: Constituents present in little amounts; ++: Constituents present in moderate amounts; +++: Constituents present in abundance; −: Constituents not detected.
Source:
a = Buhian, et.al., 2016
b = Sangi, et al., 2008.
c = Widyawati and Budiant, 2014

Some of the factors affecting the results were the kind of leaf, the type of plant, plant location, local climate, genetics of the plant and weather when the research was performed. The following table shows whether each natural antibacterial source had an active antibacterial compound. After identifying each active compound on the cherry leaf (*Muntingia calabura*), sirih leaf (*Piper betle Linn)* and beluntas leaf (*Pluchea indica L.*) here is the Table 2 explaining effectiveness from each leaf to its bacterial activity.

Table 2. The comparison of inhibited zone from natural antibacterial against *Salmonella typhimurium and Staphylococcus aureus*.

Natural antibacterial extract	Inhibited zone (mm) on bacteria	
	Staphylococcus aureus	*Salmonella typhimurium*
Cherry leaf	37.7[a]	19[a]
Beluntas leaf	15.9[c]	9.5[b]
Sirih leaf****	17[d]	16[d]

Source:
a = Buhian et.al., 2016
b = Nurhalimah et al., 2015
c = Manu, 2013
d = Madduluri et al., 2013

Cherry leaf was an effective natural antibacterial source because it had a larger inhibition zone (37.7 mm and 19 mm) which implied it occupied the “very strong” and “strong” category as compared with beluntas leaf (9.5 and 15.9 mm) and sirih leaf (17 mm and 16 mm). Another reason as to why *Muntingia calabura*was more efficient in destroying bacterial cells was because as indicated in Table 1 this leaf had more constituent saponins (+++). Saponins were observed to destroy the bacterial cell wall and opened the way for other active compounds gain entry into the bacterial cell. The more the saponins, the easier antibacterial can enter into the bacteria cell. This was another improvement to the results shown in Table 2 with each leaf tested with the same method of extraction by ethanol.

Table 3 offers a further explanation about inhibition zones

Tabel 3. Antimicrobial inhibition zone category

Diameter (mm)	Growth of inhibit response
> 20	Very strong
10-20	Strong
5-10	Medium
<5	Weak

Source: Mahardika et al., 2014

The results of the inhibition zone from leaf extracts in Table 2 compared with results in Table 3 means each natural antibacterial shows effectiveness against *Staphylococcus aureus.* Cherry leaf was shown to be very strong; beluntas leaf was also strong as was sirih leaf. When it came to the inhibition zone of natural antibacterials against *Salmonella typhimurium*, results showed thatchery leaf was very strong, beluntas leaf occupied showed medium strength, and sirih leaf was also strong. The inhibited zone was used as a parameter to measure the effects of the purported antibacterial or antimicrobial against bacteria or microbes. Another case in a hatchery farm was the case of egg shells infected by *Staphylococcus aureus* and *Salmonella spp.*

Usually, farmers in Indonesia used chemical antibacterial to solve the problem. In this research, a comparison between synthetic antibacterial and natural antibacterial on egg hatchability and mortality shows that a natural approach is better than an artificial one. To prove that natural antibacterial also had the ability to solve the problem in the hatchery farm, Table 4 elaborates further.

Table 4. The amount of hatchability and mortality on duck egg with chemical antibacterial and natural antibacterial.

Antibacterial	Hatchability (%)	Mortality (%)
Chemical antibacterial[a]	80.81	18.87
Cherry leaves extract[a]	87.74	12.26
Beluntas leaves extract[b]	44.05	55.95
Sirih leaves extract[c]	46.43	47.62

Source:
a = Alkhakim et.al. (2016) duck egg
b = Zamzamy et al., 2014
c = Nandhra et al., 2015

From the table above, it can be concluded that from among plant leaves extract and other natural resources; cherry leaf can be used as an alternative natural antibacterial in place of chemical antibacterial. Cherry leaf extract is more effective than other alternatives on hatchability amounting to 87.74% effectiveness. This result for efficiency was higher than chemical antibacterial (80.81%). Other natural antibacterials gave results as follows; Beluntas leaf (44.05%) and Sirih leaf (46.43%). This counted as low hatchability when compared with Cherry leaf.

Anderson (2012) mentioned that the bacteria *Staphylococcus aureus* and *Salmonella spp.* were commonly found in egg shells. Both of these bacteria cause failure of hatching through the death of the embryo (Soeripto and Poeloengan, 1991). Therefore, the disinfection process on hatching duck eggs should be done.

The process of egg hatching disinfection usually used formaldehyde or formalin as a disinfectant. Disinfectants can be fatal leading to the death embryos and increase abnormality when an excessive dose is used (Nandhra et al., 2015). This was confirmed by Zamzamy et al. (2015) who stated that disinfection with chemicals at low concentrations could not kill pathogenic bacteria on eggs, while when at too high concentrations, it can kill the embryo eggs. Therefore, it is necessary that herbal ingredients that can replace the function of formaldehyde as a disinfectant be used. Cherry leaf extract can slow down and kill pathogenic bacteria on eggs if used correctly.

Mechanism of action of *Muntingia-calabura* against bacteria

Extract of the cherry leaf was more effective on *Staphylococcus aureus* than *Salmonella typhimurium*. The reason for this result was that antibacterial readily attacks Gram-positive bacteria (*Staphylococcus aureus*) than gram-negative bacteria (*Salmonella typhimurium*) and also has a correlation with bacterial cell structure. The outer membrane of gram-negative bacteria acts as the entry barrier compounds where the cells are not needed, such as bacteriocins, enzymes, and compounds that are hydrophobic. The antimicrobial compounds can penetrate lipopolysaccharide (LPS) from the cell wall. Hydrophilic molecules find it easier to pass LPS compared with hydrophobic molecules. Gram-positive bacteria do not have LPS, and this means that the barrier function does not exist, and molecular antimicrobial compounds that are hydrophilic and hydrophobic (such as essential oils) can diffuse into such cells quickly (Ousallah et al., 2006).

The work of an antibacterial is divided in every bacterial cell part. The first section of the bacteria cell is the cell wall. The active compound which has a role in disturbing the bacteria cell wall is saponins because it destroys the cell wall and opens the way for other active compounds to gain entry into the bacterial cell. Turgor in the cell wall is disturbed by saponins, the effect of this interference makes the antibacterial compound to enter the bacterial cell quickly and then hampers the metabolism leading to the collapse of the bacterial cell wall. Saponins can damage bacteria cell membranes by increasing cell permeability then causing membrane proteins denaturation until lysis occurs and they are broken (Karlina et al., 2013; Johnsonet al.,2016; Ahmad et al., 2015).

The second part of the bacteria cell is the cell membrane. Steroids and flavonoids can damage this layer. Steroids kill the bacteria cell by destroying the plasma membrane of the microbial cell until it creates risk in the cytoplasm. The conditions needed for effect by steroid molecules are included in the non-polar (hydrophobic) and polar (hydrophilic) groups. This was a reason this active compound has surfactant effects that can dissolve phospholipid plasma membranes. According to Wiyanto (2010), the phospholipid is the dominant compound of the plasma membrane. Steroids inhibit the growth of bacteria such as *Staphylococcus aureus, E. coli, Proteus*

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vulgaris, Salmonella typhimurium, Klebsiella, Pneumonia dan *Bacillus subtillis* (Solomon et al., 2014; Retnowati et al., 2011). Flavonoids have three mechanisms that provide antibacterial effects. One is by inhibiting the synthesis of nucleic acids, the second is by inhibiting the function of the cytoplasmic membrane, and the third is by inhibiting the energy metabolism of the cell (Cushnie and Lamb, 2005). The bacteria that are exposed flavonoids will lose cell permeability. The cessation of metabolic activity will make bacterial cells die (Soedibyo, 2004; Kurniawan et al., 2013).

The third part in the bacterial cell is the cytoplasm. This is the most important part of the cell because it contains elements which bacteria need for survival. The cytoplasm is made up of proteins, amino acids, sugars, nucleotides, salts, vitamins, enzyme, DNA, ribosomes and internal bacterial structure that float around in the cytoplasm. The active compounds that can disturb cytoplasm are tannin, steroids, flavonoid, glycoside, and alkaloids. Flavonoids have a disinfectant effect and denature proteins which in turn cause a stop in the activity of bacterial cell metabolism. This condition happens because the enzyme (which is the protein) is catalyzed to all cell metabolism activity. Hydroxyl groups present in the structure of flavonoid compound cause changes in organic components and nutrients transport which will lead to toxic effects on bacteria (Sabir, 2005). These conditions may cause the death of a bacteria cell.

Tannin compound can inhibit protease enzyme activity, inhibit enzyme inside the sheath of bacterial cell transport leading to further destruction or inactivation of genetic material. More tannin can shrink the bacterial cell wall, destroying cell permeability and affecting cell growth and activities causing growth abnormality or the complete death of the bacteria cell (Mahardika et al., 2014; Ngajow et al., 2013). Glycoside has many functions including being an antibacterial, an anticancer and animmune-stimulant (Kusuma et al., 2005). Steroids can destroy bacteria cell membrane including the cytoplasm. The steroid molecule includes non-polar (hydrophobic) and polar (hydrophilic).These conditions make the active compound enter the cytoplasm easily (Wiyanto, 2010). The alkaloid componentis known as the DNA intercellulator, and it inhibits the bacterial cell topoisomerase enzyme (Karou et al., 2005; Mahanani et al., 2012; Retnowati et al., 2011). Topoisomerase is an enzyme for DNA replication, if this enzyme is interrupted, bacterial cells cannot reproduce.

CONCLUSION

Cherry leaf (*Muntingia calabura*) has the potential to be used as a natural antibacterial against *Staphylococcus spp.* and *Salmonella spp.* This plant is rarely used in Indonesian society. Based on the results of this review study, it is hoped that people in Indonesia will benefit by using cherry leaf as a natural antibacterial instead of chemical antibacterials.

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