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Inhibition Biofilm of Medicinal Plants: A Review

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ABSTRACT
Nowadays there is rising threat of multi-drug resistant bacteria mainly occurring due to the indiscriminate use of antibiotics. The bacteria tend to aggregate on many surfaces forming 3D structures called biofilms which are akin to the tissue organization of higher organisms. These biofilms help the bacteria regarding the spread of antibiotic resistance and increase in their pathogenicity. These biofilms are maintained by a signalling network known as quorum signalling. QS is dependent upon the presence of auto & trans-inducers which affect bacterial transcription. Hence the aim of many researchers is to inhibit QS. In this regard, medicinal plants have become important and the aim of this review is to highlight the role of QS in biofilm formation and the plants which can inhibit QS. Proper identification of plants having such roles could be a potential strategy to target multi drug resistant bacteria in future studies.

Keywords
N-Acyl Homoserine Lactone (AHL), Bacteria, Biofilms, Medicinal plants, Multi-drug resistance, Phyto-chemicals, Phyto-molecules, Quorum sensing

1. INTRODUCTION
Throughout the history of life on Earth, organisms have changed according to the changing times. The oldest organisms on Earth are found from the kingdom Monera, of which eubacteria are the most famous. Eubacteria coordinate their activities with higher order organisms by the expression of genes of the Quorum sensing (QS). The system of QS is involved in providing antibiotic resistance & pathogenicity [1-5]. QS modulate the creation of biofilms, which is the cause of antibiotic resistance & chronic infection. The rise of multi-antibiotic resistance has been linked to the role of biofilms, catalysing the search for newer anti-bacterial agents. In this regard, plants with its rich source of phyto-chemicals could prove to be a nemesis for biofilms. In this review paper, a brief overview of the QS system, its mode of functioning and the phyto-chemicals have been discussed as strategies to target QS pathway [6].

The QS system involves production of molecules known as "auto-inductors" which after reaching a particular concentration & interacting with regulators of transcription, allows specific group of gene expression. For example, the synthesis of an auto-inductor, N-acyl homoserine lactone (AHL) is dependent upon its transcriptional & post-transcriptional regulations. AHL is used for signalling by the Gram negative bacteria while a 2 component sensor employing oligopeptides are being employed by Gram positive bacteria (Figure 1 & 2) [7].

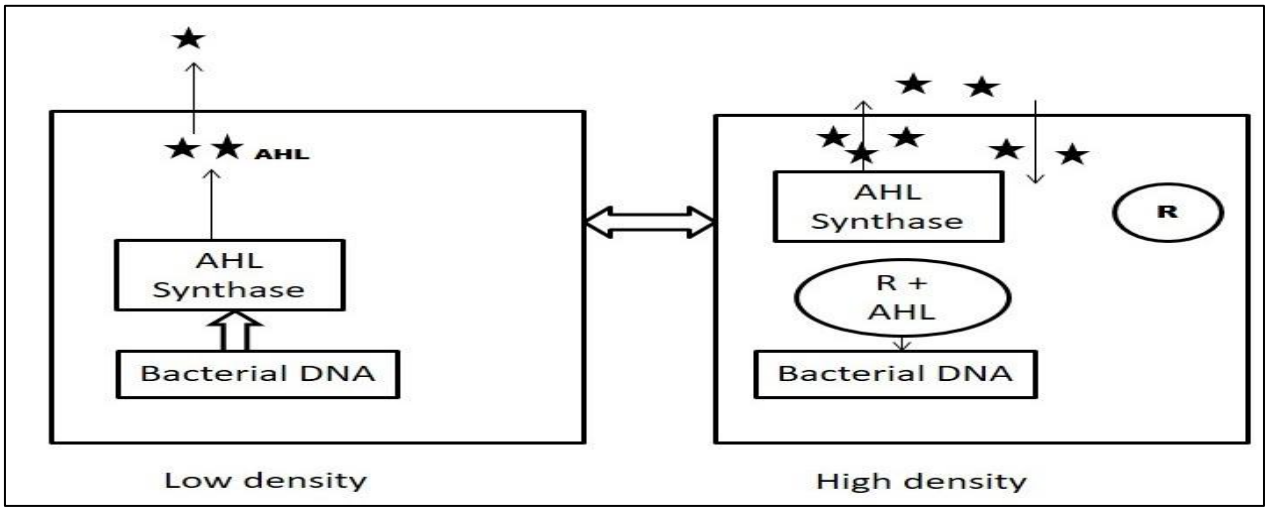

Figure 1: Gram-ve bacteria showing Quorum sensing. AHL-synthase catalyses the formation of AHL which is an auto-inducer. At low amount, by an ATP-dependent process of transport, AHL molecules enter the cytoplasm from the external medium whereas passive diffusion occurs at high concentration of AHL in the medium. AHL upon reaching a threshold level (Quorum State), interacts with R, a regulatory protein acting as a regulator of transcription. The complex of R-AHL then attaches to the target genes' promoter thereby initiating transcription dependent upon the density of bacteria .AHL - N-acyl homoserine lactone, R-AHL – R protein AHL complex[8]

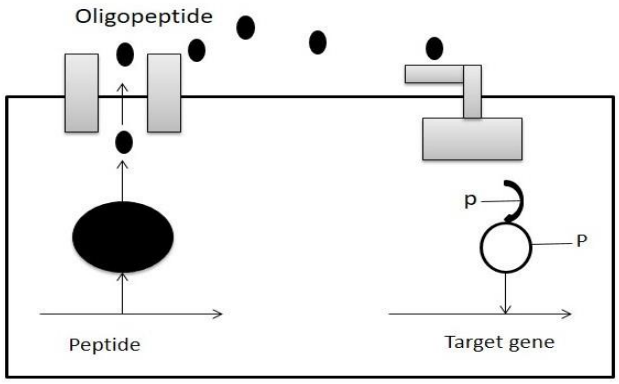

Figure 2: Quorum sensing in Gram-positive bacteria. Oligopeptides are auto-inducers in Gram positive bacteria that have been post-translationally changed by the coupling ofisoprenyllactone/ thiolactone & lanthionine. These auto-inducers are then noted by transmembrane proteins that transduce the signals via a phosphorylation avalanche. The deviations are detected by the 2-component receiver which ensures signal specificity[9]

2. LITERATURE REVIEW

Abdelhakim Bouyahya in his recent study discussed about the Infectious illnesses which are traditionally treated using chemicals and are designed to kill or limit bacterial growth. Bacterial drug resistance is a major public health problem. Now novel therapeutic objectives have been deciphered apart from the bacterial wall. Quorum sensing or bacterial pheromones are the chemicals known as the bacterial auto-inducer, to control certain processes like antibiotic resistance and the production of biofilms [10-14]. The often observed development of antimicrobial compound resistance is a key issue of this technique. The objective of this study is therefore to give an updated review of the quorum-sensing system in bacterial substances by disclosing its involvement in biofilm formation and antibiotic resistance development and by updating their relevance as a prospective natural substance target [15].

Anouk Van't Padje in recent study discussed about the relationship between mycorrhizal shrubby fungus and their host plants. The study looks at how partners transmit specific information via directional signals and highlights studies on the issue of dishonest signals [16].

W Robert McMaster in his study discuss that protozoal parasites, like other prokaryotic and viral infections, are being reported to control host cells through epigenetic changes of the host genome, altering transcription and corresponding signalling cascades. With these results, we are investigating the function of epigenetics in downregulating the Leishmania host macrophages, which may lead to irreversible inactivation and hence promote the survival of pathogenic diseases [17].

3. DISCUSSION

3.1 Dependence of QS on different pathways

3.1.1. QS Dependent on AHL Molecules

Pseudomonas aeruginosa being a gram-negative bacterium, the QS process is maintained by the RHLR-I &LasR-I systems and the enzyme “lactone synthase (luxI)” catalyses the creation of AHL. Once the bacterial cells reach a critical mass (quorum) then the AHL in the medium seeps into the cells and interact with various transcriptional factors. There is a creation of two AHL molecules form, C4- HSL & 3OC12-HSL in P. aeruginosa where each molecule binds to their precise transcription regulator (like LasR to 3OC12-HSL and RHLR to C4-HSL). The complexes so formed further activate many regulators of transcription like toxA, lasI&lasB (Figure 1) [18].

3.1.2. QS Dependent on Peptide Secretion

Auto-inducing oligopeptides (AIPs) are employed as QS by gram positivebacteria who are family members of the agrD family of gene. When the threshold level of extracellular AIPs is reached which is dependent upon the bacterial cell density, they bind to the membrane-bound agrC receptor which auto-phosphorylates agrA thereby setting up a cascade needed for the expression of agrBDCA proteins. This in turns activates the protease & toxin secretion of the bacterial cells (Figure 2) [19].

3.1.3. QS Dependent on Production of AI-2 System

Furanosyl borate diester (AI-2) is a signalling molecule found both in Gram psoitive and gram negative bacteria depending upon the threshold cell density & concentration. The production of AI-2 is conducted by a metalloenzyme called luxS from an ancestral molecule called as S-adenosylhomocysteine. Moreover, luxS-controlled Operon is influenced by phosphorylation of AI-2[20].

3.2 Formation of biofilms linked to pathogenicity of microbes:

Biofilm is a dynamic population of microorganisms bonded to a region and controlled by the release of a protective & adhesive platform. It is akin to the tissue structure in higher organisms. Two factors are important in biofilm formation. A solid surface where a 3D structure of biofilm is formed & another criteria are the poorly described transcriptional factors[6,7].

3.3 Targeting of QS pathway to tackle bacterial pathogenicity:

In order to counter the growing multi-drug resistance in bacteria, anti-QS molecules are being searched. These QS molecules help to inhibit generation, or diffusion and also promotes inhibition of signal (Figure 3 & 4).

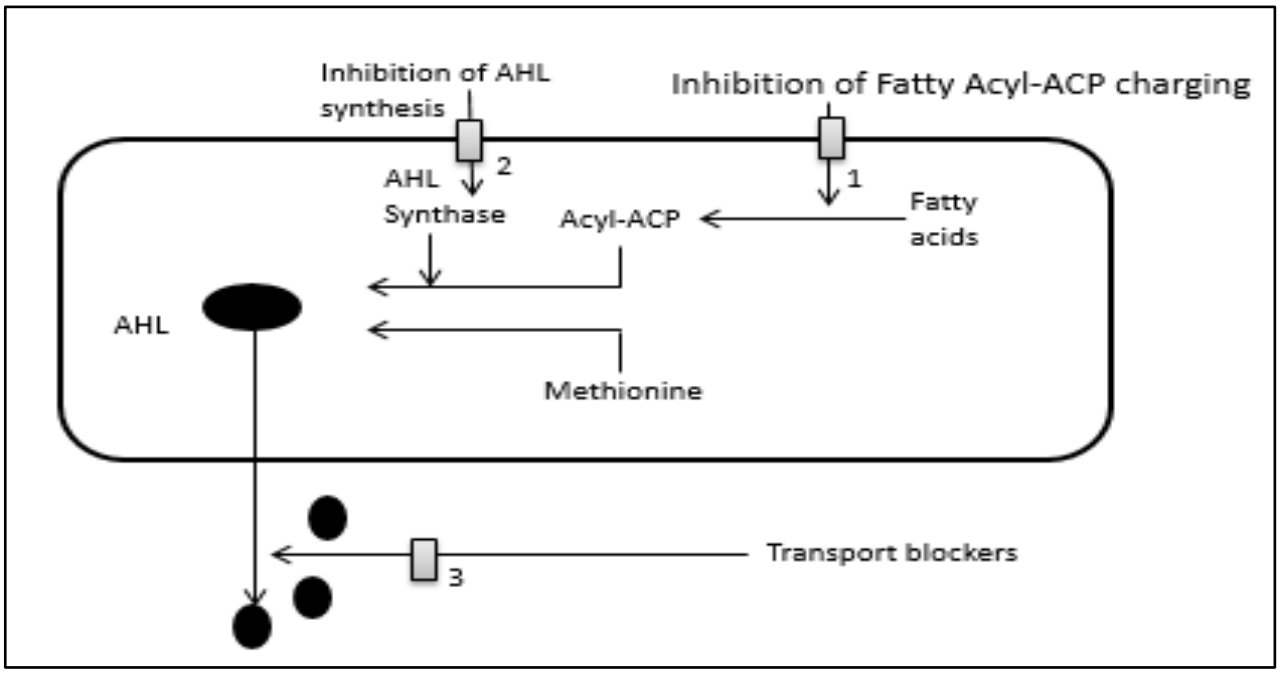

Figure 3: Inhibiting AHL signal production inhibits quorum sensing signalling occurring by 3 modes: 1) Synthesis for acyl carrier protein- fatty acyl (acyl-ACPs; AHL synthase's substrate) is inhibited 2) Synthesis N-acyl homoserine lactone (AHL) is directly inhibited 3) AHL transport inhibited[16]

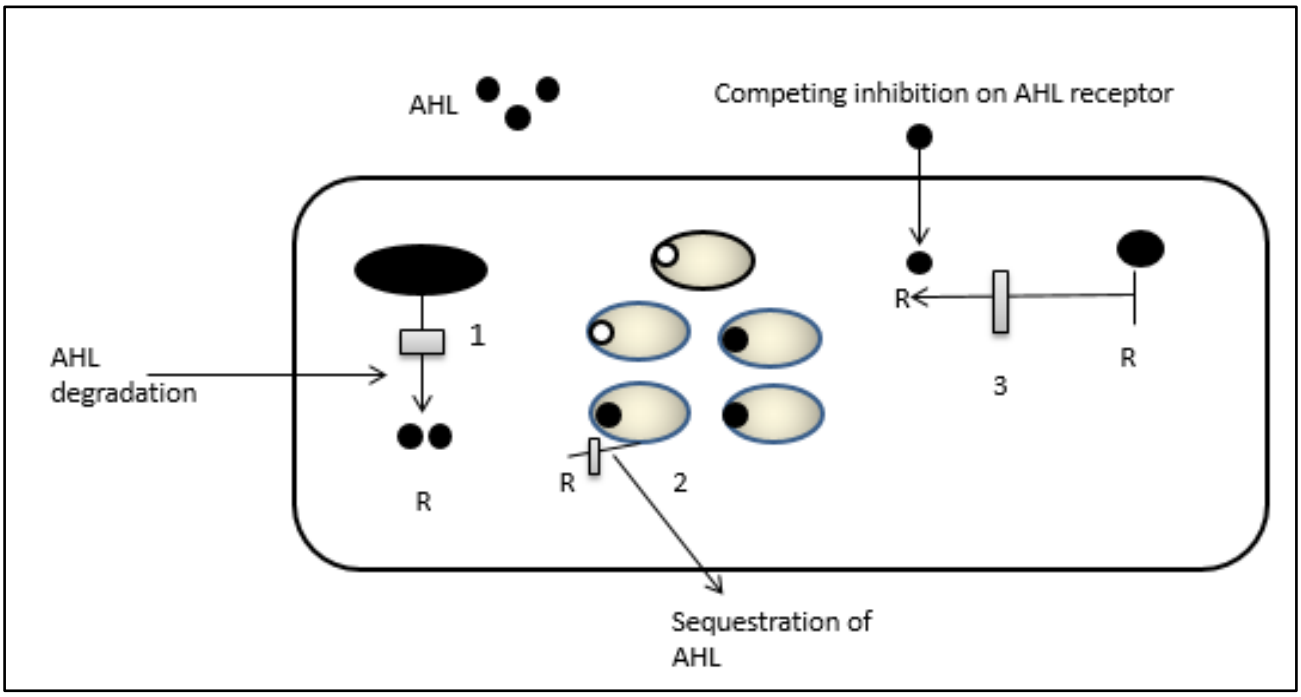

Figure 4: Signal reception being affected by inhibition of quorum sensing. Quorum sensing signal is inhibited by: 1) AHL degradation, 2) AHL sequestration 3) presence of AHL mimetic compounds [17]

3.4 Retardation of QS by phyto-molecules or phytochemicals:

The phyomolecules have been reported to have many medicinal value. Phyto-molecules are divided into following classes of chemistry: polyphenols, alkaloids, terpenes&coumarins. Flavonoids &terpenoids even at low amounts can act against bacterial membranes, cell walls & the electron transport system. Moreover the organic extracts of plants having medicinal value have been also reported to have medicinal value(9)(19). There are also reports of phyto-molecules acting against QS molecules leading to a reduction in biofilm formation. In table 1, the list of phyto-molecules isolated from plants having anti-bacterial roles owing to QS inhibition have been discussed. In (Figure 5), the anti-QS role of Curcumin has been illustrated. Here, Curcumin is shown to inhibit biofilm formation, factors that are dependent on

QS, inhibition of QS pathway genes & its interface with the environment. Curcumin is thus been reported to inhibit biofilms [19].

In (Figure 1), Quoram sensing in gram negative bacteria has been illustrated. The enzyme AHL-synthase catalyses the formation of AHL (N-Acyl homoserine lactone), an auto-inducer. At low amount, by an ATP-dependent process of transport, AHL molecules enter the cytoplasm from the external medium whereas passive diffusion occurs at high concentration of AHL in the medium. AHL upon reaching a threshold level (Quorum State) interacts with R, a regulatory protein acting as a regulator of transcription. The complex of R-AHL then attaches to the target genes' promoter thereby initiating transcription dependent upon the density of bacteria. In Figure 2, Quorum sensing in Gram-positive bacteria has been illustrated. Oligopeptides are auto-inducers in Gram positive bacteria that have been post-translationally changed by the coupling of isoprenyllactone/ thiolactone & lanthionine (21–25). These autoinducers are then noted by transmembrane proteins that transduce the signals via a phosphorylation avalanche. The deviations are detected by the 2-component receivers which ensure signal specificity. In Figure 3, Inhibiting AHL signal production inhibits quorum sensing signalling by 3 modes has been illustrated: 1) Synthesis for acyl carrier protein- fatty acyl (acyl-ACPs; AHL synthase's substrate) is inhibited 2) Synthesis N-acyl homoserine lactone (AHL) is directly inhibited 3) AHL transport inhibited. In Figure 4 illustrates that signal reception is affected by inhibition of quorum sensing by: 1) AHL degradation, 2) AHL sequestration 3) presence of AHL mimetic compound.

In (table 1), compounds isolated from plants having anti-quorum sensing roles has been tabulated. Plants traditionally known for their anti-bacterial roles are selected for bio-guided assay isolation of compounds having anti-bacterial roles. Of late, there is a great deal of interest in the phyto-molecules isolated from plants that have been traditionally reported to have anti-bacterial properties[15].

Table 1: Compounds isolated from plants having anti-quorum sensing roles. Plants traditionally known for their anti-bacterial roles are selected for bio-guided assay isolation of compounds having anti-bacterial roles [9,15]

Species of plant	Compound's name
Vanilla planifolia	Vanillin
Cedrus deodara	Taxifolin
Eridodictyon californicum	Eriyodictol
Cruciferous	3-indolyacetonitrile
Armoracia rusticana	Iberin
Brassica oleraceae	Erucin
Ajoene	Allium sativum
Hottuynia cordata	Hottuynin
Citrus sinesis	Naringin
Citrus sinesis	Naringenin
Citrus sinesis	Kaempferol
Citrus sinesis	Quercetin
Citrus sinesis	Rutin
Citrus sinesis	Hesperidin
Citrus sinesis	Apigenin
Citrus sinesis	Neoheperidin
Citrus sinesis	Neoeriocitrin

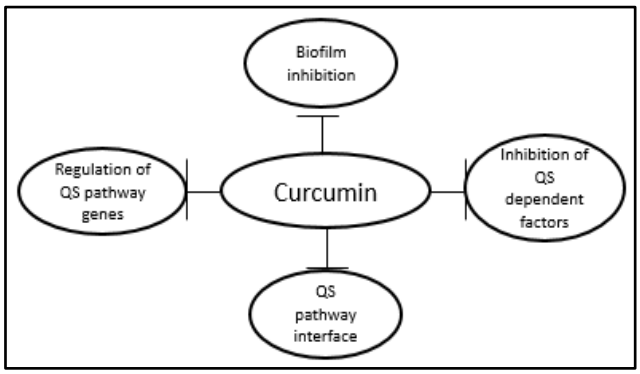

Figure 5: Curcumin targeting quorum sensing (QS). There are many reports of Curcumin being a medicinally valuable phyto-molecule isolated from Curcuma longa. Here, Curcumin is inhibiting biofilm formation, inhibiting factors dependent on QS, inhibition of QS pathway genes & interface [17]

4. CONCLUSION

Biofilms are formed due to the presence of Quorum signalling and help in establishing of microbial communities over hard surfaces. Biofilms have been blamed for the rise of multi-drug antibiotic resistant bacteria as these bacteria tend to transfer antibiotic resistance genes among themselves. Biofilms are formed akin to tissues in higher organisms. Biofilms are formed as a bacterial community on solid surfaces and help in the occurrence of pathogenicity and antibiotic resistance. Biofilm formation is dependent upon the role of quorum signalling which is dependent upon a chain of auto and trans inducers that affect bacterial gene transcription. In order to counter QS, many medicinal plants have been discovered having anti-bacterial roles and the aim of this paper is to highlight the role of QS in biofilm formation & the medicinal plants that can be used to counter it. The present study provides brief description about the various mechanisms of quorum sensing that lead to formation of biofilms and also regarding the plants having the ability to prevent the formation of biofilms. The proper identification of phyto-molecules that inhibit QS leading to decrease in formation of biofilms would certainly help in the industrial scale production of

such anti-bacterial phyto-molecules thereby helping to fight against multi-drug resistant bacteria.

REFERENCES

[1]. Rana A. Facebook Marketing and its Influence on Consumer Buying Behaviour in Kathmandu. J Bus Soc Sci Res. 2018;
[2]. Keegan BJ, Rowley J. Evaluation and decision making in social media marketing. Manag Decis. 2017;
[3]. Copuš L, Čarnogurský K. Intercultural marketing: Culture and its influence on the efficiency of Facebook marketing communication. Manag Mark. 2017;
[4]. Importance of Strategic Social Media Marketing. Expert J Mark. 2017;
[5]. Zhu YQ, Chen HG. Social media and human need satisfaction: Implications for social media marketing. Bus Horiz. 2015;
[6]. Padje A van t., Whiteside MD, Kiers ET. Signals and cues in the evolution of plant-microbe communication. Current Opinion in Plant Biology. 2016.
[7]. Li YH, Tian X. Quorum sensing and bacterial social interactions in biofilms. Sensors. 2012.
[8]. Loh J, Pierson EA, Pierson LS, Stacey G, Chatterjee A. Quorum sensing in plant-associated bacteria. Current Opinion in Plant Biology. 2002.
[9]. Waheed H, Hashmi I, Khan SJ, Kim SR, Arshad M, Nasir H. Microbial population dynamics and profiling of quorum sensing agents in membrane bioreactor. Int Biodeterior Biodegrad. 2016;
[10]. Felix R, Rauschnabel PA, Hinsch C. Elements of strategic social media marketing: A holistic framework. J Bus Res. 2017;
[11]. Duffett RG. Influence of social media marketing communications on young consumers' attitudes. Young Consum. 2017;
[12]. Ferrández-Pastor FJ, García-Chamizo JM, Nieto-Hidalgo M, Mora-Pascual J, Mora-Martínez J. Developing ubiquitous sensor network platform using internet of things: Application in precision agriculture. Sensors (Switzerland). 2016;
[13]. Ryu M, Yun J, Miao T, Ahn IY, Choi SC, Kim J. Design and implementation of a connected farm for smart farming system. In: 2015 IEEE SENSORS - Proceedings. 2015.
[14]. Kiran US, Arya S, Rajasekaran M. Design and implementation of smart and low cost multi-task farming system using Arduino. Int J Eng Technol. 2018;
[15]. Bouyahya A, Dakka N, Et-Touys A, Abrini J, Bakri Y. Medicinal plant products targeting quorum sensing for combating bacterial infections. Asian Pacific Journal of Tropical Medicine. 2017.
[16]. Struss AK, Pasini P, Flomenhoft D, Shashidhar H, Daunert S. Investigating the effect of antibiotics on quorum sensing with whole-cell biosensing systems. Anal Bioanal Chem. 2012;
[17]. Robert McMaster W, Morrison CJ, Kobor MS. Epigenetics: A New Model for Intracellular Parasite-Host Cell Regulation. Trends in Parasitology. 2016.
[18]. Jolivet-Gougeon A, Bonnaure-Mallet M. Biofilms as a mechanism of bacterial resistance. Drug Discovery Today: Technologies. 2014.
[19]. Bouyahya A, Bakri Y, Khay EO, Edaoudi F, Talbaoui A, Et-Touys A, et al. Antibacterial, antioxidant and antitumor properties of Moroccan medicinal plants: A review. Asian Pacific J Trop Dis. 2017;
[20]. Lee J, Wu J, Deng Y, Wang J, Wang C, Wang J, et al. A cell-cell communication signal integrates quorum sensing and stress response. Nat Chem Biol. 2013;
[21]. Choi S, Kim J, Ryu M, Yun J, Miao T, Ahn I-Y, et al. Design and Implementation of a Connected Farm for Smart Farming System FIESTA-IoT View Project Design and Implementation of a Connected Farm for Smart Farming System. IeeexploreIeeeOrg. 2015;
[22]. McHenry MP. Agricultural bio-char production, renewable energy generation and farm carbon sequestration in Western Australia: Certainty, uncertainty and risk. Agriculture, Ecosystems and Environment. 2009.
[23]. Spugnoli P, Dainelli R. Environmental comparison of draught animal and tractor power. Sustain Sci. 2013;
[24]. Bentsen NS, Felby C, Thorsen BJ. Agricultural residue production and potentials for energy and materials services. Progress in Energy and Combustion Science. 2014.
[25]. Guthiga PM, Karugia JT, Nyikal RA. Does use of draft animal power increase economic efficiency of smallholder farms in Kenya? Renew Agric Food Syst. 2007;

