2020: Volume 11, Issue 4

Review Article

The Importance of Ultrasound Findings in Children with Acute Abdominal Pain to Prevent Unnecessary Surgery

Herlina Uinarni, Conny Tanjung, Huldani, Aminuddin Prahatama Putra, Mashuri, Bayu Indra Sukmana, Heru Wahyudi, Abdullah Zuhair, Aderiel Gabrian Tarius, Wisnu W

SRP. 2020; 11(4): 377 - 383

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.56

Review Article

Genetically Determined ABO and (Rh) Rhesus Blood Groups and Their Associations with Diabetes Mellitus

Louay Al-Ani, Huda M. Mahmood, Noor Abdulhaleem

SRP. 2020; 11(4): 604 - 608

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.90

Review Article

Correlation Analysis on Religiosity Level against LGBT Perception as Deviation Form

Asti Melani Astari, Kurnia Laksana, Qomariyatus Sholihah, Wahyudi Kuncoro, Yati Srihayati.

SRP. 2020; 11(4): 21 - 26

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.05

Review Article

Effect of Total Cholesterol Levels and Triglycerides on Blood Pressure Hypertension Patients Overview against Puskesmas Banjar Ethnic Group in Cempaka Banj

Huldani, Siti Kaidah, Dwi Laksono Adiputro, Harun Achmad, Bayu Indra Sukmana, Deby Kania Tri Putri, Yusrinie Wasiaturrahmah, Renie Kumala Dewi, Didit Aspriyanto, Prahatama Putra, Anastasya Deborah M. C Manik, Ketrin Zailin, Ika Kusuma Wardani

SRP. 2020; 11(4): 384 - 389

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.57

Review Article

Spectrophotometric and Colorimetric Determination of Pharmaceutical by Oxidative Coupling Reaction: A Review

Aseel M. Aljeboree

SRP. 2020; 11(4): 609 - 615

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.91

Review Article

Isolation and Identification Fungi Caused Rot of Capsicum annum Fruit and Study Ability to Produce Protease and Lipase

Hiba Hadi Taha, Adeba Younis Shareef, Eman Mohamad Taher.

SRP. 2020; 11(4): 27 - 31

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.06

Review Article

A Review of Bandotan Leaf Extract (Ageratum conyzoides L.) in Inhibition Test to the Growth of Bacteria (Porphyromonas gingivalis) Case of Periodontitis Disea

Harun Achmad, Andi Mardiana Adam, Aulia Azizah, Bayu Indra Sukmana, Huldani, Shafira Nurul Khera, Yunita Feby Ramadhany

SRP. 2020; 11(4): 390 - 395

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.58

Review Article

Therapeutic Effect of Pumpkin (Cucurbita pepo L.) on Post Burn Injury in White Mice

Hazima Mossa Alabassi, Zahraa Hussein M. Kadri, Maha A. Gathwan, Yasamine J. Kadem, Zahraa K. Kadhim

SRP. 2020; 11(4): 616 - 620

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.92

Review Article

Comparison between Effects of Ketamine and Remifentanil Used During Oocyte Retrieval on ICSI Outcome
Hameedah Abdul Hussein Mohsin, Raad Ghazi Reshan, Mufeeda Ali Jawad
SRP. 2020; 11(4): 621 - 628

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.93

Review Article

Role of Demographic Factors and Stakeholders in Determining the Marketing Strategies of Pharmaceutical Companies in Thailand
Sunisa Pensap, Witthaya Mekhum.
SRP. 2020; 11(4): 45 - 51

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.09

Review Article

Preparation of Inhalable Salbutamol Proliposome Using Different Core Carriers and Investigate the Impact of Simulated Lung Fluid Use in Evaluation
Basma Yahya Al-Najjar, Mowafaq M. Ghareeb
SRP. 2020; 11(4): 629 - 639

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.94

Review Article

How the Innovation Take Place in Pharmaceutical Industry?: An Empirical Investigation from Thailand
Chaidet changpia, Pornkul Suksod, Withilak Chantanasombat.
SRP. 2020; 11(4): 52 - 59

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.10

Review Article

Extragenital Pathologies of Pregnant Women in the Southern Regions of The Republic of Kazakhstan
L.M. Aktaeva, D.D. Mirzakhmetova, Z.Padaiga
SRP. 2020; 11(4): 405 - 412

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.61

Review Article

The Impact of Inflation, Investment, Population and FDI on Economic Growth through Supply Chain Performance in Pharmaceutical sector of Thailand
Nichanant Sermsri, Witthaya Mekhum.
SRP. 2020; 11(4): 60 - 66

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.11

Review Article

Study of Metabolism of Bone in Iraqi Children with GH Deficiency Before and After 6 months GH Replacement Therapy
Mithal R. Alkubaisi, Hameed Hussein Ali, Fakhri J. Al-Dalla Ali, Abbas M. Rahmah
SRP. 2020; 11(4): 640 - 651

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.95

Review Article

The Impact of Life-style Drugs on Society: An Empirical Evidence from Pattaya, Thailand
Natnaporn Aeknarajindawat, Nattachai Aeknarajindawat, Damkerng Aswasuntrangkul.
SRP. 2020; 11(4): 67 - 74

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.12

≫ Abstract ≫ PDF

Review Article

The Indicators Leading to Tuberculosis (Tb) Under-Reporting in Public Hospital of Kudus

Rusnoto, Bhisma Murti, Reviono, Noor Cholifah, Rizka Himawan, Ahmad Nur Syafiq, Sofia Februanti

SRP. 2020; 11(4): 656 - 659

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.97

Review Article

Organization of Interventional Arrhythmological Care in The Republic Of Kazakhstan

M.K.Bapayeva, A.B.Almukhanova, M.A.Kamaliyev, G.Zh.Tokmurzieva, A.N.Nurbakyt, B.A. Ryssmendiyev, Z.Padaiga

SRP. 2020; 11(4): 419 - 421

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.63

Review Article

Does Excessive Alcohol Consumption Increase Economic Cost? An Investigation from Thailand

Supattra Pranee, Jongdee Phusalux, Watchrin Sangma, Naiyana Wongjunya.

SRP. 2020; 11(4): 88 - 93

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.15

Review Article

Reproductive and Therapeutic Editing of Human Genes and Gene Modification of Plants and Animals in Terms of Legislation and Research Activity Restrictions i

Ksenia Michailovna Belikova

SRP. 2020; 11(4): 422 - 430

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.64

Review Article

Estimation of Pollination in Mahogany Revealed by Microsatellite Markers : Case in South Sulawesi, Indonesia

Siti Halimah Larekeng, Gusmiaty, Yuni Fitri Cahyaningsih, Mirza Arsiaty Arsyad, Wanti Mustika Sari, Muhammad Restu, Astuti Arif

SRP. 2020; 11(4): 660 - 673

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.98

Review Article

Supply Chain Risk Factors and Corporate Repute in Pharma Industry of Thailand

Chonmapat Torasa, Witthaya Mekhum.

SRP. 2020; 11(4): 94 - 101

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.16

Review Article

Some General Remarks and Legal Restrictions in Reproductive and Therapeutic Gene Modification in Russia

Ksenia Michailovna Belikova

SRP. 2020; 11(4): 431 - 439

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.65

Review Article

Supply Chain Management and Its Influence on the Performance of Pharmaceutical Companies

Thammarak Srimarut, Witthaya Mekhum.

SRP. 2020; 11(4): 102 - 110

≫ Abstract ≫ PDF

Review Article

Transmissional and Magical Nature of Naming System
Zhanna O. Tektigul, Ainura B. Bayadilova-Altybayeva, Kulzat K. Sadirova, Gulmira, K.Kushkarova
SRP. 2020; 11(4): 445 - 450

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.67

Review Article

Does Empl
Agus Syab
SRP. 2020;

≫ Abstract

Review Article

Surgical Treatment of Renal Cancer with Tumor Thrombus of the Inferior Vena Cava in a Patient after Exploratory Laparotomy
M.S. Mauletbayev, A.K. Makishev, S.B. Irimbetov, D.N. Ahmedin, N.M. Dzhantemirova
SRP. 2020; 11(4): 451 - 455

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.68

Review Article

Building Nurses? Organizational Commitment by Providing Good Quality of Work Life
Diana, Anis Eliyana, Alvin Permana Emur, Ahmad Rizki Sridadi.
SRP. 2020; 11(4): 142 - 150

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.22

Review Article

Safety Leadership and Safety Behavior in MRO Business: Moderating Role of Safety Climate in Garuda Maintenance Facility Indonesia
Erman Noor Adi, Anis Eliyana, Hamidah, Aprilia Tri Mardiana.
SRP. 2020; 11(4): 151 - 163

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.23

Review Article

Synbiotic (PoultryStar® Sol) Protects Rat Liver from Oxidoreductive Stress Induced by T2-Mycotoxicity
Ajwad Awad Muhammad Assumaidaee, Nathera M. Ali, Zaid O Ibraheem
SRP. 2020; 11(4): 456 - 467

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.69

Review Article

Topical Minoxidil Alone and with Topical Lanoprost in Localized Alopecia Areata Treatment: Comparative Study (2019-2020)
Ahmed Abdulhussein Kawen.
SRP. 2020; 11(4): 164 - 168

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.24

Review Article

Effect of Lawsonia and Thuja Extract on Hemolysin from Staphylococcus aurous which Isolate from Tonsillitis
Mohammed abdul aziz ismail, Farkad Hawas Musa, Abdullah .H.Alkhater
SRP. 2020; 11(4): 468 - 470

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.70

Review Article

Review Article

Information Sharing, Joint Reward System, leadership Style and Supply Chain Responsiveness: Mediating role of Cross-Functional Coordination
Masnilam Hasibuan, Yusro Hakimah, Agusta Linda, Nirmala Haty Harahap, Fithra Maharani
SRP. 2020; 11(4): 731 - 738

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.107

Review Article

Effect of W
Samir Mish
SRP. 2020;

≫ Abstract

Review Article

A CAPACITATED HETEROGENEOUS VEHICLE ROUTING PROBLEM FOR PHARMACEUTICAL PRODUCTS DELIVERY
Asrin Lubis, Herman Mawengkang
SRP. 2020; 11(4): 738 - 741

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.108

Review Article

Molecular Study of Some Virulence Factors and Antimicrobial Susceptibility Pattern of Citrobacter frundii Isolated from Human Diarrhea
lham A. Bunyan.
SRP. 2020; 11(4): 195 - 201

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.28

Review Article

Determination of Influencing Factors for Slope Stability Using Grey Relational Analysis (GRA) Technique
Ashanira Mat Deris, Badariah Solemon, Hairin Taha, Rohayu Che Omar.
SRP. 2020; 11(4): 202 - 206

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.29

Review Article

PARENTA
Masruroh i
SRP. 2020;

≫ Abstract

Review Article

The Effectiveness of Direct and Indirect Feedback on Learners? Writing Performance across Different Gender and Cultural Background
Sabarun, Aris Sugianto, Tazkiyatunnafs Elhawwa.
SRP. 2020; 11(4): 207 - 216

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.30

Review Article

New Skewness Correction S Control Chart for Monitoring Dispersion of Skewed Data with Application in Healthcare
A.M.A., Atta, S.S. S. Yahaya, Z. Zain, N. Ahmad.
SRP. 2020; 11(4): 217 - 222

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.31

Review Article

Immunohistochemistry Study Urothelial Carcinoma using Tumor Markers (EGFR, EMA and CD117)
Ebtihal Chiad Abass, Alaa Salah Jumaah, Kaswer Musa Jaafar Altoriah, Hawraa Sahib Al-Haddad, Aseel Al-Quzweni, Hussein Raof Alghaszali, Najah R. Hadi.

Review Article

The Protective Effects of Achillea fragrantissima on Immune Response in Mice Model: A Pilot Study
Abbas M. Al-Sarraf, Yasmeen Ali Hussien, Yahiya Ibrahim Yahiya, Hayder A. Al-Aubaidy.
SRP. 2020; 11(4): 243 - 246

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.35

Review Article

THE BEHAVIOR OF MUSLIM INVESTORS IN INVESTING IN STOCKS ON THE INDONESIA STOCK EXCHANGE DURING THE COVID-19 PANDEMIC
Sugianto, Muslim Marpaung, Siti Mujiatun, Ismail Husein, Purnama Ramadani Silalahi
SRP. 2020; 11(4): 745 - 752

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.109

Short Communication

Synthesis, Characterization of Ibuprofen N-Acyl-1,3,4-Oxadiazole Derivatives and Anticancer Activity against MCF-7 Cell Line
Mustafa Q. Ali Alderawy, Leaqaa A. Raheem Alrubaie, Falah Hassan Sheri
SRP. 2020; 11(4): 681 - 689

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.100

Review Article

Formative Research to Develop a Workplace Physical Activity Program in Vietnam: Protocol for a Mixed Method Study
Van Dinh Tran, Nguyen Tu Quyet, Hoang Hai, Phan Dang Than, L& 432;u Phuong Dung, Tran Ngoc Phuong Mai, Le Thi Phuong Mai, Xuong Tuyet Nguyen.
SRP. 2020; 11(4): 247 - 251

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.36

Short Communication

The Recurrence Rate of Odontogenic Keratocyst after Enucleation with Peripheral Ostectomy
Ammar Luay Alshibib, Hassanien A. Al-jumaily, Ahmed Fadhel Alquisi
SRP. 2020; 11(4): 690 - 694

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.101

Short Communication

The Effect of Temperature and Storage Time on the Concentration of Vitamin D in Human Serum
Asmaa Y. Al-Baitai, Saifaldeen M. Abdalhadi, Suhad A. Ibrahim, Ali A. Ali, Ghassan H. Alzamily
SRP. 2020; 11(4): 695 - 700

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.102

Review Article

Efficiency of Double Vaccine by Azotobacter chroococcum & Pseudomonas chlororaphus on Some Biological characteristics of Hordeum vulgare
Shaimaa Mohe Dawd, Shaimaa Hajalan Sayer, Nbaa Mutea Abid Al-Alh
SRP. 2020; 11(4): 476 - 481

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.72

Short Communication

Introducing Silver Nanoparticles as Anti-Giardial in Experimentally Infected Mice: Therapy versus Toxicity
Ekhlas M. Idan, Naksheen M. Ardalan, Zahra'a A. Ahmed
SRP. 2020; 11(4): 701 - 708

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.103

Review Article

Review Article

The Manag
E.T. Toleu,
SRP. 2020;

≫ Abstract

Short Communication

Synthesis and Antimicrobial Activity of New Nitric Oxide-Donor Containing Compounds
Nagham M. Zaki Dawood, Banan Borhan Saeed, Zahraa Sedeeq Qasim
SRP. 2020; 11(4): 719 - 724

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.105

Review Article

Analytical
Galyna Me
SRP. 2020;

≫ Abstract

Review Article

Phytochem
Ni Kadek V
SRP. 2020;

≫ Abstract

Short Communication

Removal of Brilliant Dyes from its Aqueous Solution by Adsorption on Siliceous Rocks
Afiaa Abdul Rassol Abdul Kareem, Ammar Jasim Mohammed
SRP. 2020; 11(4): 725 - 730

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.106

Review Article

Formulation of Ethanol Extract (Myrmecodia pendans) as an Antibacterial Streptococcus mutans in Chewable Lozenges for Children with Early Childhood Carie
Sri Ramadhany, Muhammad Harun Achmad, Hendrastuti Handayani, Maria Tanumihardja, Marhamah F. Singgih, Nur Hildah Inayah, Yunita Feby Ramadhany.
SRP. 2020; 11(4): 252 - 257

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.37

Review Article

The Effect of White Shrimp Head Chitosan Gel (Litopenaeus vannamei) on Inhibitory Strength of Periodontopathogenic Bacteria and Accelerating Wound Healin
Asdar Gani, Nurlindah Hamrun, A. Mardiana Adam, Ermina Pakki, Harun Achmad, M Husni Cangara, Husnul Khatimah Maulidina, Rezqy Maelani, Dewiayu Dewang.
SRP. 2020; 11(4): 258 - 267

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.38

Review Article

Analysis of VDR Gene Polymorphism in Beta Thalassemia Major (Beta Thalassemia Major / Vitamin D / Calcium / 825T/T Vitamin D Receptor Gene)
Eriska Riyanti, Muhammad Harun Achmad, Mieke Hemiawati Safari, Meirina Gartika, Yunita Feby Ramadhany.
SRP. 2020; 11(4): 268 - 274

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.39

Review Article

Effect of the Combination of Demineralization Freeze Dried Dentin Matrix (DFDDM) and Moringa Oleifera Lam on Nuclear Factor Kapa B as a Marker of Bone
Arni Irawaty Djais, Sri Oktawati1, Hasanuddin Thahir, Muchammad Hatta, Bayu Indra Sukmana, Nurdiana Dewi, Huldani, Yayah Inayah, Widodo, Irene Edith Riewpassa,
SRP. 2020; 11(4): 515 - 522

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.78

Harun Achmad, Maria Tanumihardja, Sartini, Sri Ramadhany, Marhamah F. Singgih, Yunita Feby Ramadhany, Nurul Mutmainnah.
SRP. 2020; 11(4): 293 - 299

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.42

Review Article

Basic Adaptation Mechanisms of the Woman?s Body Ensuring Intrauterine Fetal Growth
Alina E.Markina, Margarita V.Labzina, Elena N.Kovalenko, Ella V.Romanova, Elena A.Alyamkina, Olga V.Slugina.
SRP. 2020; 11(4): 300 - 305

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.43

Review Article

Research Reviews on Effect of Exercise on DAMP?s, HMGB1, Proinflammatory Cytokines and Leukocytes
Huldani, Ilhamjaya Pattelongi, Muhammad Nasrum Massi, Irfan Idris, Agussalim Bukhari, Agung Dwi Wahyu Widodo, Harun Achmad.
SRP. 2020; 11(4): 306 - 312

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.44

Review Article

Assessment of Hypoglycemic Effect of an Oral Insulin Formulation in Chickens as an Experimental Animal Model
Ali M Janabi, Suaad Traiji Zamil, Suhad Traiji Zamil, Hussein Abdulkadhim A
SRP. 2020; 11(4): 531 - 542

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.80

Review Article

Association between Natural Killer Cell Cytotoxicity and the Progression of Non-Small Cell Lung Cancer
Nasser Ghaly Yousif, Kareem G.Mohammed, Samar Muayad Mohammed, Najah R. Hadi, Fadhil G. Alamran, Song Zheng, Maitham G. Yousif, Jillen Lee, Jonthan Adrienne
SRP. 2020; 11(4): 543 - 551

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.81

Review Article

Antibacterial Activity of Allium sativum against Streptococcus mutans ATCC 25175 in Indonesia
Eriska Riyanti, Ani Melani Maskoen, Roosje Rosita Oewen, Naninda Berliana Pratidina, Harun Achmad, Yunita Feby Ramadhany.
SRP. 2020; 11(4): 313 - 318

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.45

Review Article

Using Fourier Transform Infrared (FTIR) Spectroscopy Coupled with Multivariate Analysis to Diagnose Polycystic Ovary Syndrome (PCOS)
Afrah Mohammed Hassan Salman, Mohammed A. Al-Zubaidi, Maysaa Ali Abdul khaleq
SRP. 2020; 11(4): 552 - 560

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.82

Review Article

Inhibit of the Virus Infections by using Aromatic Oils, Saccharomyces cerevisiae, Boswellia Carterii and Zinc
Wisamjasim Abed Ali, Huda Raheem Hashim
SRP. 2020; 11(4): 561 - 569

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.83

Review Article

Antioxidant and Antitumor Activities of Methanolic Extracts Obtained from Red Delicious and Granny Smith Apples' Seeds
Yasser Fakri Mustafa, Eman Tareq Mohammed, Raghad Riyadh Khalil
SRP. 2020; 11(4): 570 - 576

Identification and Antimicrobial Susceptibility of Granulicatella adiacens Isolated from Periodontal Pocket
Harun Achmad, Andi Mardiana Adam, Surijana Mappangara, Sri Oktawati, Rizalinda Sjahril, Marhamah F. Singgih, Ingrid Neormansyah, Heri Siswanto
SRP. 2020; 11(4): 324 - 331

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.47

Review Article

Identification and Antimicrobial Susceptibility of Granulicatella adiacens Isolated from Periodontal-Pocket
Harun Achmad, Andi Mardiana Adam, Surijana Mappangara, Sri Oktawati, Rizalinda Sjahril, Marhamah F. Singgih, Ingrid Neormansyah, Heri Siswanto
SRP. 2020; 11(4): 324 - 331

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.47

Review Article

Collaborative Governance Framework in Health Care: A Qualitative Exploration of Hospital Pharmacy Management Reform at Hospital Setting in Indonesia
Hardi Warsono, Retna Hanani, Halim Dwi Putra.
SRP. 2020; 11(4): 337 - 338

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.49

Review Article

Study of Carcinoma Embryonic Antigen (CEA) and its Relationship to TSH Polymorphisms in Patients with Thyroid Gland Dysfunction.
Sawsan Hassan Kadhum
SRP. 2020; 11(4): 580 - 582

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.86

Review Article

Pharmacy Service Quality for Pharmacy Customer Satisfaction, Trust, and Loyalty
Teddy Chandra, Layla Hafni, Gressy Novita
SRP. 2020; 11(4): 342 - 347

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.50

Review Article

Globalization and Problems of Modern Regional Economy
Varvara Raphaelovna Markaryan, Litvina Kristina Yakovlevna, Kamchatova Ekaterina Yurevna, Chernova Vera Alexandrovna, Kozhushko Elena Anatolyevna
SRP. 2020; 11(4): 348 - 353

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.51

Review Article

Interleukin-6 Associated with Insulin Resistance in Non-Diabetic Predialysis Chronic Kidney Disease Patients
Rendy Revandana Bramantya, Chandra Irwanadi Mohani, Soebagijo Adi Soelistijo
SRP. 2020; 11(4): 354 - 358

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.52

Review Article

Study the Laser Bleaching for Several Human Teeth and Their Structural Properties as a Model of Therapy
Dhurgham M.Abd Ali AL- Haddad, Mithaq M. Mehdy Al- Sultani
SRP. 2020; 11(4): 583 - 592

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.87

Review Article

Comparison of the 25(OH)D Levels Between Sarcopenia and Frailty in Elder Women: A Cross-Sectional Observation Analytic Study in Elderly Community in Sur
Viranti Ayu Adyanita, Novira Widajanti, Sony Wibisono

Review Article

A Case of I
Yu.V. Zbrue
SRP. 2020;

≫ Abstract

Review Article

Differences in VO2 Max Based on Age, Gender, Hemoglobin Levels, and Leukocyte Counts in Hajj Prospective Pilgrims in Hulu Sungai Tengah Regency, South Ka
Huldani, Harun Achmad, Aryadi Arsyad, Aminuddin Prahatama Putra, Bayu Indra Sukmana, Dwi Laksono Adiputro, Julia Kasab.
SRP. 2020; 11(4): 9 - 14

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.03

Review Article

Sequence-based Detection and Identification Biodiversity of Uncultivated Fungi in Soils.
Wijdan Ahmed Ali
SRP. 2020; 11(4): 599 - 603

≫ Abstract ≫ PDF DOI: 10.31838/srp.2020.4.89

Review Article

Analysis of Dental Caries & Gingivitis with the Occurrence of Stunting in Children in Makassar City (Tamalanrea Subdistrict)
Harun Achmad, Hendrastuti Handayani, Marhamah F. Singgih, Sherly Horax, Sri Ramadhany, Fedelia Setiawati, Yunita Feby Ramadhany
SRP. 2020; 11(4): 371 - 376

Editorial Board

Editor-in-Chief

Editorial Board

How to Cite:
Rivani, E., Arfijanto, M. V., & Widodo, A. D. W. (2022). Vancomycin for methicillin-resistant staphylococcus aureus biofilm eradication is associated with the emergence of heterogeneous vancomycin intermediate staphylococcus aureus. *International Journal of Health Sciences*, *6*(S9), 811–818. https://doi.org/10.53730/ijhs.v6nS9.12536

Vancomycin for methicillin-resistant *staphylococcus aureus* biofilm eradication is associated with the emergence of heterogeneous vancomycin intermediate *staphylococcus aureus*

Erizka Rivani
Department of Microbiology, Faculty of Medicine, Sriwijaya University, Palembang, South Sumatera, Indonesia, Department of Clinical Microbiology, Faculty of Medicine, Airlangga University/Dr. Soetomo General Academic Hospital, Surabaya, East Java, Indonesia
Corresponding author email: rivanierizka@gmail.com

Muhammad Vitanata Arfijanto
Department of Internal Medicine, Faculty of Medicine, Airlangga University/Dr. Soetomo General Academic Hospital, Surabaya, East Java, Indonesia

Agung Dwi Wahyu Widodo
Department of Clinical Microbiology, Faculty of Medicine, Airlangga University/Dr. Soetomo General Academic Hospital, Surabaya, East Java, Indonesia

***Abstract*---**Vancomycin is the first-line therapy for MRSA infections, even though the standard dose is inadequate for biofilm eradication. This study aimed to asses the efficacy of vancomycin in eradicating biofilms and the influence of exposure on the emergence of hVISA isolates. The biofilm formed by MRSA isolates was exposed to vancomycin concentrations of 1 times the MIC, 1,000 times the MIC, and 10,000 times the MIC; exposed continously for 24 hours vs intermittently for 6 hours/day for 3 days. Measurement of the optical density of the biofilm was carried out to determine the percentage of biofilm eradication. Biofilm specimens exposed to vancomycin were subcultured onto BHIA-VC selective media to isolate hVISA. The highest biofilm eradication effect was found in isolates exposed to vancomycin at a concentration of 10,000 times the MIC. Vancomycin exposure correlated with the emergence of hVISA isolates, especially after exposure to low concentrations of vancomycin. For optimum eradication of MRSA biofilms, vancomycin concentrations exceeding 1.000 times the MIC are required. Exposure to vancomycin at a dose

Manuscript submitted: 9 April 2022, Manuscript revised: 18 June 2022, Accepted for publication: 27 July 2022

equal to one-times the MIC had no effect on biofilm eradication and was associated with the emergence of MRSA isolates with decreased susceptibility to vancomycin.

***Keywords*---**MRSA, biofilm eradication, vancomycin, hVISA.

Introduction

Methicillin-resistant *Staphylococcus aureus* (MRSA) is one of the leading causes of persistent bacterial infections in humans (Silva et al., 2021). MRSA is a pathogen that causes mild community-related infections such as skin and soft tissue infections as well as serious infections in hospitals, such as pneumonia, osteomyelitis, brain abscess, and sepsis, with significant morbidity and mortality rates (Cascioferro et al., 2020). In addition to antibiotic resistance, which complicates the treatment of MRSA infections, MRSA's ability to form biofilms makes it one of the major causes of nosocomial and device-related infections (El-Hamid et al., 2020).

Biofilm-forming bacteria have such a tolerance to antibiotics, the body's immune system, and environmental stress due to extracellular matrix protective mechanisms and changes in metabolic rate and growth rate, which makes it challenging to treat biofilm-caused infections (Boakye et a.l, 2018; Sharma et al., 2019). The release of the device in an attempt to eliminate the source of infection is the primary action in cases of device-related biofilm infection, but this is not always possible, therefore antibiotics are sometimes the only treatment option (Silva et al., 2021).

Vancomycin is a glycopeptide antibiotic that is the main choice for treating MRSA infections. Experiments in vitro and in vivo have demonstrated that the minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) of sessile cells in biofilms are 10-1,000 times greater than those of planktonic cells (Algburi et al., 2017; Cascioferro et al., 2021). Vancomycin has a complex molecular structure and a large size; in vitro studies reveal that its biofilm penetration ability is 64%, which is relatively lower than that of other antibiotics with activity against MRSA (Kaneko et al., 2021). Local administration of antibiotics can increase concentrations of antibiotics at the site of infection with minimal serum antibiotic concentrations and be developed as a therapeutic modality for biofilm-associated infections (Ciofu et al., 2017).

The efficacy of local antibiotics in treating MRSA infections has been extensively studied, yet their clinical application remains limited. One issue impeding its clinical implementation is the concern of increasing resistance rates due to the use of high doses of local antibiotics (Haas and Schultz, 2010). In this study, the authors attempted to eradicate MRSA biofilms by subjecting them to vancomycin and evaluating the effectiveness of eradication as well as the effect of in vitro exposure on the emergence of hVISA/VISA isolates.

Method

Study design

Experiments were conducted on ten MRSA isolates from Clinical Microbiology Laboratorium Dr. Soetomo General Academic Hospital and two standard reference isolates (ATCC MRSA 43300 and ATCC *S. aureus* 25923 KWIK-STIK® Microbiologics). The experiment included the identification of MRSA isolates that produce biofilms and proved that they were not hVISA isolates as evidenced by no growth on brain-heart infusion agar with 4 µg/ml vancomycin and 16 mg/ml casein (BHIA-VC) selective media, followed by a biofilm eradication test with vancomycin utilising a microtiter plate biofilm assay, and the detection of hVISA isolates from biofilm specimens after vancomycin exposure.

Ethical considerations

This study was reviewed by the Ethics Committee of the Faculty of Medicine, Airlangga University (0926/LOE/301.4.2/VI/2022).

Procedure

Twelve isolates were subcultured onto Nutrient Agar to recover bacteria from frozen stocks. The growing colonies were suspended in normal saline with a turbidity of 0.5 McFarland. The biofilm formation procedure was carried out on a microtiter plate by adding 160 µl of TSB medium, 20 µl of glucose, and 20 µl of bacterial suspension to each well, followed by a 48-hour incubation period.

After the formation of the biofilm, the biofilm eradication test was carried out with vancomycin. The media in the wells was discarded and new TSB medium was added with vancomycin solutions to achieve a concentration of 2 µg/ml, 2 mg/ml, and 20 mg/ml in the test solution/well, respectively. Vancomycin was administered for either 24 hours or 6 hours per day for three consecutive days.

After the incubation procedure complete, microtiter plates are dyed with crystal violet and their optical density was evaluated using a spectrophotometer. To identify bacterial growth from biofilms, sterile swabs were used to collect biofilm samples, which were then plated on Nutrient Agar media. Colonies grown on Nutrient Agar were subcultured into BHIA-VC media to determine the presence of hVISA/VISA isolates. The experiment was conducted for four times.

Table 1. Characteristic of research isolates

Isolate	Specimen source	Biofilm production characteristic[a]
Klinis 1	Blood	*Strong-biofilm producer*
Klinis 2	Blood	*Strong-biofilm producer*
Klinis 3	Blood	*Strong-biofilm producer*
Klinis 4	Urine	*Strong-biofilm producer*
Klinis 5	Blood	*Strong-biofilm producer*
Klinis 6	Pus	*Strong-biofilm producer*
Klinis 7	Pus	*Moderate-biofilm producer*
Klinis 8	Pus	*Weak-biofilm producer*
Klinis 9	Blood	*Weak-biofilm producer*

Klinis 10	Sputum	*Moderate-biofilm producer*
MRSA 43300	ATCC	*Weak-biofilm producer*
S.aureus 25923	ATCC	*Weak-biofilm producer*

ATCC: *American Type Culture Collection,* MRSA: *methicillin-resistant Staphylococcus aureus.* Biofilm production characteristic is assesed from biofilm formation assay. Isolates were classified as strong biofilm producers if the optical density (OD) of the biofilm produced was four times of the negative control, moderate biofilm producers if the OD falls within the range 2-4 times of the negative control, weak biofilm producers if the OD was two times of the negative control, and non-biofilm producers if the OD was less than 0.5 times of the negative control.

Discussion

The data of optical density value and growth on the BHIA-VC media did not follow a normal distribution (Shapiro-Wilk value 0.000). In terms of percentage, the biofilm density of the test isolate was compared to the biofilm density of the positive control. The OD of isolates exposed to 2 µg/ml vancomycin was greater than the OD of the positive control (without vancomycin exposure).
The eradication of biofilm by vancomycin was determined by the following formula:

$$\% \text{ eradication: } \frac{\textit{Mean}\text{ OD control} - \textit{Mean}\text{ OD treatment}}{\textit{Mean}\text{ OD control}} \times 100\ \%$$

Vancomycin exposure at 2 µg/ml had no effect on biofilm eradication. Biofilm eradication rates ranged from 21 to 63.9% in the continuously exposed 2 mg/ml concentration group. Biofilm eradication in the group treated intermittently to 2 mg/ml for six hours per day for three days ranged from 32.8% to 69.2%. Biofilm eradication ranged between 60 and 87.6% in the group that was continuously exposed to 20 mg/ml. In the group that was intermittently exposed to 20 mg/ml, biofilm eradication ranged from 64 to 86.1%. The mean optical density varied significantly between exposure to vancomycin concentrations of 2 µg/ml, 2 mg/ml, and 20 mg/ml ($p<0.05$; Mann-Whitney; 95% confidence interval). The optical density measurements did not differ significantly between continuous and intermittent exposure groups ($p=0.220$; Mann-Whitney; 95% confidence interval). Vancomycin did not completely eliminate biofilm at any concentration nor incubation period.

Table 2. Optical density (OD)

Vancomycin Exposure		Isolates (OD)											
Incubation period	Concentration	1	2	3	4	5	6	7	8	9	10	11	12
Positive Control		0,49	0,43	0,28	0,25	0,24	0,19	0,14	0,13	0,12	0,15	0,10	0,08
24 hours	2 µg	0,91	0,50	0,37	0,24	0,29	0,243	0,15	0,135	0,12	0,165	0,13	0,09
	2 mg	0,18	0,25	0,13	0,13	0,19	0,07	0,06	0,07	0,08	0,08	0,06	0,06
	20 mg	0,08	0,10	0,08	0,08	0,08	0,06	0,02	0,04	0,04	0,02	0,02	0,03
Positive Control		0,89	0,84	0,92	0,65	0,71	0,46	0,42	0,40	0,45	0,52	0,76	0,32
6 hours/day for 3 consecutive days	2 µg	1,31	1,18	0,93	0,79	0,86	0,57	0,46	0,50	0,41	0,69	0,84	0,33
	2 mg	0,60	0,50	0,28	0,30	0,32	0,19	0,17	0,18	0,15	0,28	0,31	0,21
	20 mg	0,29	0,30	0,13	0,17	0,17	0,09	0,08	0,10	0,08	0,18	0,11	0,09

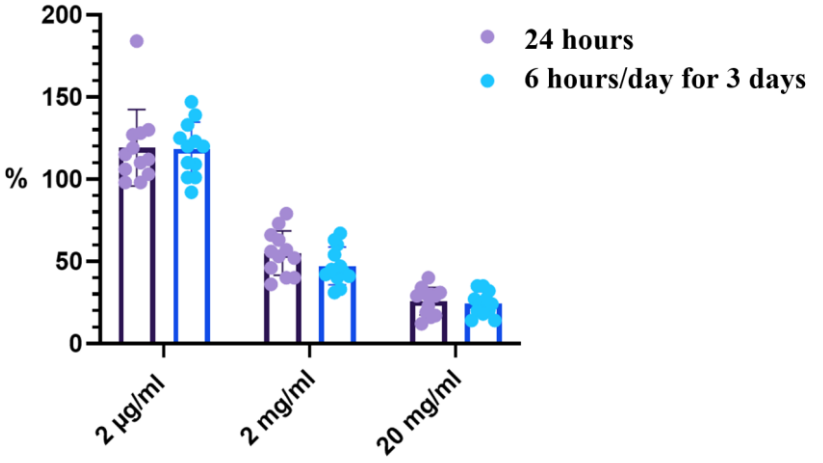

Figure 2. Percentage of biofilm density following exposure to vancomycin (compared to positive control)

After vancomycin exposure to its biofilm, three isolates grew on BHIA-VC medium. The highest incidence of hVISA isolation occurred in the group exposed to 2 µg/ml vancomycin, followed by the group exposed to 2 mg/ml vancomycin, and finally the group subjected to 20 mg/ml vancomycin. The concentration of vancomycin corresponded with the subsequence emergence of hVISA (p=0.046; cross-tabulation; 95% confidence interval).

There was no statistically significant difference in the effect of the emergence of hVISA isolates based on time of exposure (p=0.333; cross-tabulation; 95% confidence interval). However, growth in BHIA-VC media was more common in those exposed to vancomycin for 6 hours each day and incubated for 72 hour (intermittent exposure).

Table 3. Growth on BHIA-VC media

Vancomycin Exposure		Isolat											
Incubation periode	Concentration	1	2	3	4	5	6	7	8	9	10	11	12
24 hours	2 µg	+	-	-	-	+	-	+	-	-	-	-	-
	2 mg	-	-	-	-	-	-	+	-	-	-	-	-
	20 mg	-	-	-	-	-	-	-	-	-	-	-	-
6 hours/day for 3 days	2 µg	+	-	-	-	+	-	+	-	-	-	-	-
	2 mg	+	-	-	-	+	-	+	-	-	-	-	-
	20 mg	-	-	-	-	-	-	+	-	-	-	-	-

(+) : growth on BHIA-VC media. (-) : no growth on BHIA-VC media

The eradication of biofilms by vancomycin was evaluated using a microtiter plate biofilm assay in accordance with the procedure published by Haney et al. in 2021. In this study, the percentage of MRSA biofilm eradication after exposure to vancomycin at concentrations of 1 times the MIC (2 µg/ml), 1,000 times the MIC 2 (mg/ml), and 10,000 times the MIC (20 mg/ml) was determined. The rate of

eradication was evaluated by the optical density of the residual biofilm following vancomycin exposure. Optical density of MRSA biofilm between exposed group and positive control group (which was not exposed to vancomycin) was then measured.

Continuously or intermittently, the group exposed to 2 µg/ml vancomycin concentration of 1 MIC demonstrated a thicker biofilm than the positive control. MRSA isolates exposed to sub-MIC concentrations of vancomycin (1 µg/ml) showed an increase in biofilm formation through an autolysis-dependent mechanism that enhanced extracellular DNA synthesis and membrane vesicle secretion (Hsu et al., 2011; Mirani and Jamil, 2011; He et al., 2017). The biofilm penetration capacity of vancomycin is inadequate, resulting in a lower drug concentration in the biofilm layer than in the test solution (Singh et al., 2011).

The proportion of biofilm thickness varied significantly between groups treated to vancomycin concentrations of 2 g/ml, 2 mg/ml, and 20 mg/ml. The most significant difference was observed between groups exposed to one times the MIC concentration and those exposed to the other two concentrations, with the eradication effect only occurring in groups exposed to 1000 and 10,000 times the MIC. Biofilm elimination was higher when subjected to 10,000 times MIC than when subjected to 1,000 times MIC, although 100% eradication was not reached.

The percentage of biofilm thickness did not differ substantially between the groups that received continuous or intermittent vancomycin exposure for a total of 24 hours and 18 hours. Vancomycin demonstrated a partially time-dependent antibiotic profile in tests against planktonic bacteria and a time-dependent antibiotic profile in tests on mature biofilms, where concentrations of 0.2 mg/ml to 2 mg/ml were able to eradicate the total MRSA mature biofilm on metal implants after 28 days of exposure (Post et al., 2017). This study concludes that a concentration of at least 1,000 times the MIC and an exposure time of at least 18 hours, either continuously or intermittently, are required for effective biofilm eradication.

Detection of hVISA/VISA isolates employing the Satola technique in this investigation. Brain-heart infusion agar media containing 4 g/ml vancomycin and 16 mg/ml casein showed a 90% sensitivity and 95% specificity for detecting the growth of hVISA/VISA (Howden et al., 2010; Satola et al., 2011). Three of the twelve examined isolates grew in BHIA-VC selective media after vancomycin treatment, indicating the presence of the hVISA/VISA subpopulation. Through selective pressure mechanisms, exposure to glycopeptide antibiotics and beta-lactams induces hVISA by polymutations that result in alterations to the cell wall of S. aureus (Hanaki et al., 2005; Matsuo et al., 2013; Roch et al., 2014). Prior studies on the development of hVISA by in vitro vancomycin exposure used planktonic bacteria and subinhibitory concentrations. Our recent work demonstrated that exposure to extremely high doses above the MIC can still trigger the development of hVISA isolates in biofilms from sessile bacteria.

Conclusion

This study concludes that the administration of vancomycin in the treatment of biofilm-associated MRSA infection poses the risk of selection and induction of isolates with decreased susceptibility to vancomycin. Vancomycin treatment with Ireatment of vancomycin at suboptimal doses increases the probability of hVISA isolation. To achieve a near-100 percent eradication efficacy with vancomycin, up to 10,000 times the MIC is necessary, hence local antibiotic therapy regimens for MRSA-associated biofilm infections must always be adjusted.

Acknowledgments

We thank Dr. Soetomo General Academic Hospital and Department of Microbiology, Faculty of Medicine, Sriwijaya University, for providing all necessary support in this research.

References

Algburi, A., Comito, N., Kashtanov, D., Dicks, L. M., & Chikindas, M. L. (2017). 'Control of biofilm formation: antibiotics and beyond. *Applied and environmental microbiology'*, *83*(3), e02508-16.

Anchundia, M. J. L., Gámez, M. R., Quiroz, A. M. V., Miles, G. M., & Molina, L. A. V. (2022). Energy efficiency and the link with society. *International Research Journal of Management, IT and Social Sciences*, *9*(4), 398-404. https://doi.org/10.21744/irjmis.v9n4.2094

Boakye, Y. D., Osafo, N., Danquah, C. A., Adu, F., & Agyare, C. (2019). 'Antimicrobial agents: Antibacterial agents, anti-biofilm agents, antibacterial natural compounds, and antibacterial chemicals'. *Antimicrobials, Antibiotic Resistance, Antibiofilm Strategies and Activity Methods*, 75.

Cascioferro, S., Carbone, D., Parrino, B., Pecoraro, C., Giovannetti, E., Cirrincione, G., & Diana, P. (2021). 'Therapeutic strategies to counteract antibiotic resistance in MRSA biofilm-associated infections'. *ChemMedChem*, *16*(1), 65-80.

Ciofu, O., Rojo-Molinero, E., Macià, M. D., & Oliver, A. (2017). Antibiotic treatment of biofilm infections. *Apmis*, *125*(4), 304-319.

El-Hamid, A., Marwa, I., Y El-Naenaeey, E. S., Hegazy, W. A., Mosbah, R. A., Nassar, M. S., ... & Bendary, M. M. (2020). 'Promising antibiofilm agents: Recent breakthrough against biofilm producing methicillin-resistant Staphylococcus aureus'. *Antibiotics*, *9*(10), 667.

Haas, L. E., & Schultz, M. J. (2010). 'Selective decontamination of the digestive tract reduces pneumonia and mortality'. *Critical care research and practice*, *2010*.

Hanaki, H., Yamaguchi, Y., Yanagisawa, C., Uehara, K., Matsui, H., Yamaguchi, Y., ... & Nagayama, A. (2005). 'Investigation of β-lactam antibiotic-induced vancomycin-resistant MRSA (BIVR)'. *Journal of infection and chemotherapy*, *11*(2), 104-106.

Haney, E. F., Trimble, M. J., & Hancock, R. E. (2021). 'Microtiter plate assays to assess antibiofilm activity against bacteria'. *Nature Protocols*, *16*(5), 2615-2632.

He, X., Yuan, F., Lu, F., Yin, Y., & Cao, J. (2017). 'Vancomycin-induced biofilm formation by methicillin-resistant Staphylococcus aureus is associated with the secretion of membrane vesicles'. *Microbial pathogenesis*, *110*, 225-231.

Howden, B. P., Davies, J. K., Johnson, P. D., Stinear, T. P., & Grayson, M. L. (2010). 'Reduced vancomycin susceptibility in Staphylococcus aureus, including vancomycin-intermediate and heterogeneous vancomycin-intermediate strains: resistance mechanisms, laboratory detection, and clinical implications.' *Clinical microbiology reviews*, *23*(1), 99-139.

Hsu, C. Y., Lin, M. H., Chen, C. C., Chien, S. C., Cheng, Y. H., Su, I. N., & Shu, J. C. (2011). 'Vancomycin promotes the bacterial autolysis, release of extracellular DNA, and biofilm formation in vancomycin-non-susceptible Staphylococcus aureus'. *FEMS Immunology & Medical Microbiology*, *63*(2), 236-247.

Kaneko, H., Nakaminami, H., Ozawa, K., Wajima, T., & Noguchi, N. (2021). 'In vitro anti-biofilm effect of anti-methicillin-resistant Staphylococcus aureus (anti-MRSA) agents against the USA300 clone'. *Journal of Global Antimicrobial Resistance*, *24*, 63-71.

Matsuo, M., Cui, L., Kim, J., & Hiramatsu, K. (2013). 'Comprehensive identification of mutations responsible for heterogeneous vancomycin-intermediate Staphylococcus aureus (hVISA)-to-VISA conversion in laboratory-generated VISA strains derived from hVISA clinical strain Mu3'. *Antimicrobial agents and chemotherapy*, *57*(12), 5843-5853.

Merta, I. N., & Suderana, I. W. (2020). COVID-19 pandemic handling community social and cultural sector stimulus efforts. *International Journal of Social Sciences and Humanities*, *4*(3), 1–12. https://doi.org/10.29332/ijssh.v4n3.434

Mirani, Z. A., & Jamil, N. (2011). 'Effect of sub-lethal doses of vancomycin and oxacillin on biofilm formation by vancomycin intermediate resistant Staphylococcus aureus'. *Journal of basic microbiology*, *51*(2), 191-195.

Post, V., Wahl, P., Richards, R. G., & Moriarty, T. F. (2017). 'Vancomycin displays time-dependent eradication of mature Staphylococcus aureus biofilms'. *Journal of Orthopaedic Research*, *35*(2), 381-388.

Satola, S. W., Farley, M. M., Anderson, K. F., & Patel, J. B. (2011). Comparison of detection methods for heteroresistant vancomycin-intermediate Staphylococcus aureus, with the population analysis profile method as the reference method. *Journal of clinical microbiology*, *49*(1), 177-183.

Sharma, D., Misba, L., & Khan, A. U. (2019). 'Antibiotics versus biofilm: an emerging battleground in microbial communities'. *Antimicrobial Resistance & Infection Control*, *8*(1), 1-10.

Silva, V., Almeida, L., Gaio, V., Cerca, N., Manageiro, V., Caniça, M., ... & Poeta, P. (2021). 'Biofilm formation of multidrug-resistant MRSA strains isolated from different types of human infections'. *Pathogens*, *10*(8), 970.

Singh, R., Ray, P., Das, A., & Sharma, M. (2010). 'Penetration of antibiotics through Staphylococcus aureus and Staphylococcus epidermidis biofilms'. *Journal of antimicrobial chemotherapy*, *65*(9), 1955-1958.

Suryasa, I. W., Rodríguez-Gámez, M., & Koldoris, T. (2021). Get vaccinated when it is your turn and follow the local guidelines. International Journal of Health Sciences, 5(3), x-xv. https://doi.org/10.53730/ijhs.v5n3.2938