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Review on Erythromycin: A Macrolide Antibiotic

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ABSTRACT: Macrolides is a natural or semisynthetic products which exhibit their antibacterial activity primarily by reversible binding to the bacterial 50S ribosomal subunits and by blocking nascent proteins' progression through their exit tunnel in bacterial protein biosynthesis. Erythromycin is a macrolide antibiotic. It is highly effective to cure a pathogenic infection, with low side-effects and contributes in the development of second and third generation of semi-synthetic derivatives of erythromycin that further broaden its microbiological features as macrolide antibiotics. Erythromycin is active against gram-positive and negative micro-organisms. These are used in the treatment of respiratory, gastrointestinal, genital tract, skin and soft tissue infections. The development of erythromycin analogues with no antimicrobial activity but with enhanced prokinetic properties may offer additional advantages in the future. The functional significance of this nucleotide residue would havebeen eventually inferred from its repeated occurrence in mutants resistant to MLS (Macrolide Lincosamide Streptogramin) antibiotics as well as to the numerous mutations. In the antibacterial effect, erythromycin has different immune modulatory, anti-inflammatory and prokinetic activities.

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INTRODUCTIONS:

In last five decades the erythromycin is widely used in therapy despite of having its disadvantages like insolubility of water, instability in the gastric pH, bitter taste and irregular absorption from the gastrointestinal tract [1]. The erythromycin salts like erythromycin lactobionate and glucoheptonate (water soluble salts), erythromycin stearate and ethyl succinate (water insoluble salts) and erythromycin estolate (water insoluble ester salt) are used clinically which have been officially accepted by the USP [2,3]. Large inter subject variability in serum concentration (After oral administration) and in pharmacokinetic parameters (After intravenous administration) is small [4]. For this

reason, the drug is listed by the American Academy of Pharmaceutical Sciences as having serious bioavailability problems. To overcome the bioavailability problem of erythromycin, erythromycin taurate has been prepared and its physico-chemical and biological properties have been evaluated. The action of erythromycin has also been investigated for a gastrointestinal motility disorders as a Prokinetic agent and recently within the context of critically ill patients. To accelerate intraluminal transit, the contractile force increases by the Prokinetic agents and its drugs. The anti-inflammatory action may have a desirable side effect to its antibiotic action, using erythromycin A merely for its Prokinetic effect alone raises the concern about promoting emergence of macrolide resistance. There are two mechanisms of resistance to erythromycin for *S. pyogenes* target site modification and efflux mechanism [5,6]. The target site modification by two genes that is ermB or ermTR [7]. All these transferred by transposons and encode production of methylases which are methylate a certain amino acid in the ribosomal RNA of the 23S ribosomal subunit. The Macrolides lincosamide and streptogramin group B share target site so all these antibiotics have the modification results in resistance. These mechanisms are issue by two phenotypes - Macrolide Lincosamide Streptogramin constitutive resistant and Macrolide lincosamide streptogramin inducible resistant. The efflux mechanism is due to a mefA gene [8], which is also transferred by transposones and encodes production of a pump which thrusts out mainly 14 and 15 membered macrolides. Third M phenotype presents this mechanism. Isolates of different phenotypes need different treatment that by differentiation is important. Isolates of the MLS constitutive phenotype are resistant to all macrolides, lincosamides and streptogramin group B so no one can be used. For isolates, from the MLS-inducible phenotype only 16-membered macrolides can be used like spiramycin, josamycin, midecamycin. It is possible that resistance develops during the treatment course. Isolates of the M phenotype can be treated by lincosamides and 16-membered macrolides.

Dosage form of erythromycin and metabolism:

Erythromycin is available in different oral and pharmaceutical dosage forms including enteric-coated tablets, oral suspensions, ophthalmic solutions, ointments, gels and injections. Oral erythromycin combinations are erythromycin base, erythromycin estolate (contraindicated during pregnancy), and erythromycin ethyl succinate and erythromycin stearate. Erythromycin gluceptate and erythromycin lactobionate combinations are available for injection [9,10]. As erythromycin is destroyed by gastric juice, the oral formulations are given as enteric coated form. Intravenous infusion of erythromycin is characterized by high incidence of thrombophlebitis. It is metabolized in the liver by demethylation, with the formation of estolate that can cause cholestatic hepatitis, therefore its use is restricted in liver impairments [11,12]. Erythromycin is distributed to all body tissues except the cerebrospinal fluid and it crosses the placental barrier and excreted in the breast milk. The American Association of Pediatrics (AAP) is determined erythromycin is safe during the lactation period [13]. Erythromycin is the second choice following - penicillin's contraindications and allergic reactions in infectious pregnant women and it is assigned to pregnancy Category B by FDA. Erythromycin estolate may be more prone to hepatotoxicity receiving by pregnant women. Erythromycin should only be given during pregnancy when need has been clearly established [14-17]. There have reports of infantile hypertrophic pyloric stenosis (IHPS) occurring in infants erythromycin therapy [18]. Erythromycin is metabolized in the liver and its metabolites are the demethylated product at the dimethyl amino group, the noxide of the desosamine, and descladinose erythromycin, which mainly has much reduced antibacterial potency, elimination occurs in the bile and finally in the urine [19].

Macrolides and their Resistance:

During the treatment of bacterial infections, in inflammatory cells macrolide accumulation is play an important role since inflamed tissue releases a whole range of chemo attractant molecules, and polymorpho nuclear cells, which are loaded with the antibacterial agent, therefore, concentrated in the inflame tissue. Bacterial components activate and degranulation inflammatory cells. The macrolide is release into the surrounding tissue and contributing to faster clearance of the infectious pathogen [20]. The inducible and consecutive resistance phenotype as well as the macrolide resistance phenotype are differentiated with erythromycin and clindamycin discs (D test) by the double disk diffusion method [21]. Bacteria possess a large and continuously evolving variety of resistance mechanisms for antibiotics. It is concerned with the use

of macrolides and their ultimately impact on emergent resistances, particularly among streptococcal species, as they are pathogens that commonly cause infections for which macrolides are indicated and it increased the antibiotic pressure caused by macrolides and it may be linked with increased macrolide resistance in bacteria like streptococci [22-25]. It is important to understand to the use of a certain antibiotic may not be limited purely to the group of antibiotics to which it belongs to the principle that emergence of new resistances in relation. In the spread of resistant clones the cross-selection plays a crucial role; for example, Karl Kristinsson has demonstrated that the abundant usage of cotrimoxazole in Iceland has contributed to the spread of a penicillin-resistant clone of serotype 6 *S. pneumonia* [26]. It is also known that during the transfer of genetic material between isolates including *S. pyogenes*, that genes conferring resistance to macrolides can be passed on in combination with other resistance genes. For example Tet (O) conferring resistance to tetracycline's, resulting in multidrug-resistant isolates [27].

Antimicrobial Action of Erythromycin:

In bacteria at the step of chain elongation, Erythromycin A mainly prohibits the formation 50S subunit [28] and RNA-dependent protein synthesis by the reversibly binding to the 50S ribosome subunit and the blocking trans-peptidation or translocation reactions [29]. At the level of the 23S rRNA, These are inhibit messenger RNA (mRNA) translation which are mostly interacting with the five out of six domains and the ribosomal proteins L4 and L22 are part the of 50S subunit [30]. The other macrolides and antibiotics share a binding site by Erythromycin A and interference with their binding to ribosome. By the binding in the exit tunnel of the ribosome for the macrolides achieve inhibition of the protein synthesis where the evolving peptide is primarily formed by 23S rRNA. The interaction between the ribosome and the evolving peptide are take place with the tunnel is a dynamic structural component. The interactions influence the progression of synthesis and the activity of the ribosomal peptidyltransferase [31]. A constriction the exit tunnel form by the ribosomal proteins L4 and L22. The Macrolides bind in close proximity to this constriction and thus block the exit tunnel. It appears that the exact location of the protein synthesis inhibition seems to be dependent on the amino acid sequence of the evolving peptide. The ketolide such as telithromycin represent the most recent subgroup of the macrolide antibiotics. Whenever compared with the older macrolides and they demonstrate increased by binding to the ribosome [32,33]. The understanding of the structure activity relationship of the dissimilar macrolides has been appeal in description [34]. Choice when 'atypical' pneumonia, such as that caused by *Legionella pneumophila*, is suspected then the Macrolides indicated for used as drug of choice. They are an important alternative to penicillin in respiratory tract infections, [35] infections caused by groups C and G streptococci, *S. pneumoniae* and *S. pyogenes* and for rheumatic fever prophylaxis [36, 37]. They are used drugs on a large scale in the treatment of the streptococcal and respiratory tract infections. Ketolides retain activity against Gram-positive isolates resistant to erythromycin A and used in the treatment of respiratory tract infection [30]. On the target site of ribosomal interaction in ketolides differs from the other macrolides due to the own different molecular structure, and therefore they appear unaffected by some currently known mechanisms of resistance [38].

Mode of action of erythromycin A on the gastrointestinal system:

Erythromycin A has a gastrointestinal motility stimulating effect. The macrolide resistance antibiotics also have the stimulating effect on the gastrointestinal system. These are act like a motilin receptor agonist in the gut and gallbladder over 20 years [39, 40]. Migrating myoelectric complex has a phase of stimulate enteric nerves and smooth muscle and triggering [41,42]. Erythromycin A in humans are mediated via different pathways affected by antral motor. The induction of premature activity front is mediated by the activation of an intrinsic cholinergic pathway. While via a pathway potentially involving activation of a muscular receptor of the induction of enhanced antral contractile activity may be mediated [43]. In studies Erythromycin A may have different effects with different doses in patients with the diabetic gastro paresis [44]. erythromycin A elicited a premature phase 3 complex that started in the stomach and migrated to the small intestine with 40 mg dose, while doses of 200 and 350 mg erythromycin A got a burst of antral phase-3-like contractions and that did not migrate to small intestine, prolonged period of antral contractile activity was followed.

Erythromycin A as a prokinetic agent:

Gastric emptying has been investigated by the use of the Prokinetic agents in a range of clinical endpoints of

critical care patients and these are beyond the scope of this article For example, erythromycin A shortened the prolonged gastric-emptying times for liquids and solids to normal in patients with insulin-dependent diabetes mellitus and gastroparesis suggesting that it may have therapeutic value in patients with severe diabetic gastroparesis [44,45]. It is shown potential benefit in the other areas after vagotomy [46] and the patients with the chronic intestinal pseudo-obstruction [47]. These application could have an impact is in the critical care setting in the several area. The successful and early administration of enteral nutrition is integral to the improving of the clinical outcome, in fewer septic complications, decreased bacterial gut translocation and catabolic response to injury and improved wound healing in the result [48-50]. The main two studies which is success rate increases of small-bowel-feeding-tube placement and shortens procedure time is compared with placebo erythromycin A have [51, 52] and the other study did not find any significant and advantage of erythromycin A over metoclopramide in this setting and concluded that motility agents were given prior to the tube insertion as well as do not augment advancement of the feeding tube beyond the stomach and in fact hinder placement into the duodenum [53]. In numerous studies, shown the evaluating gastrointestinal motility by measuring the acetaminophen absorption and performing manometry and breath testing have shown. These are impaired in the critically ill, with the decreased the gastric emptying and diminished migrating motor complexes [54-56]. In the mechanically ventilated patients the Slow gastric emptying, and gastro paresis, is a major limitation. In addition to impairing the absorption of nutrients and drugs, can lead to complications directly related to the enteral feeding, such as bacterial overgrowth and esophageal reflux. These types of the complications place these patients on risk of pulmonary aspiration, pneumonia and sepsis, which is in turn, impacts on mortality [57]. By the overcoming of the gastrointestinal dysmotility the prokinetic agents improve tolerance to enteral nutrition [50, 58]. Their usefulness in the critical care population has been reviewed [59, 60]. This type class of drugs which includes the non-antibiotics in addition to erythromycin was found to have a beneficial effect on gastrointestinal motility as measured by endpoints such as gastric residuals, acetaminophen absorption as a surrogate marker and manometry in certain situations during the enteral feeding. Therefore, it is recognized the number and sample sizes of clinical trials. The ideal doses of the drugs are to be established while this area was small. On the clinical outcomes including the incidence of pneumonia and mortality rate [61] the motility agents have the one randomized trial of to date has assessed with their impact and these did not show the any type benefit of the prokinetic over placebo.

Booth, *et al*. [59] found the two small studies in their review investigation. Erythromycin A is compared with placebo on gastrointestinal transit and feeding tolerance with effects of with sample populations range from 10 to 20 [62, 63]. Increased the absorption and antral contractions and reduced the residual volumes, by the use of acetaminophen as a surrogate maker. It has not a significant effect on the gastric microbial overgrowth [64] through erythromycin, and that associated with patients being shown in a category like successful feeders. Erythromycin A is promote gastric emptying only for the first 3 days of interal feeding for another larger placebo controlled trial of 40 patients demonstrated. But after sometime the residual volumes have no important effect [65].

Preclinical studies:

***In vitro Selection of Erythromycin*:**

Resistance 8Cj1199 and NCTC11168 were the subjected to step-wise-step selection in the Mueller Hinton agar plate containing erythromycin. During the first step, the cells were plated on the mueller hinton (MH) agar which containing 0.25 µg/ml erythromycin. After the 3 to 5 days of incubation under microaerophilic condition at 42 ºC. Colonies were selected and repeated incubated more than four to five times with same concentration of the erythromycin. By the first-step the mutant was obtained and then by exposing the cells subjected to next step selection to a twofold increased concentration of erythromycin. This procedure of selection was repeated up to 10 times to obtain highly erythromycin-resistant mutants. By using the broth micro dilution method all the *in vitro*selected mutants were subjected to MIC test.

***In vitro studies*:**

In vitro antimicrobial spectrum minimum inhibitory concentration (MIC) and in pharmacokinetic parameters in rabbit, for the derivative include *in vitro* antimicrobial potency. According to the Indian Pharmacopoeia [66] Erythromycin was used as reference standard for the above studies. The *in vitro* antimicrobial potency was determined by different following method i.e. Grove and Randall [67] using Sarcinalutea ATCC 9341 as the test

organism. By the single point assay method [66] the concentration of erythromycin taurate was obtained. The standard curve was prepared and used as an erythromycin base. The zone of inhibition was obtained by Erythromycin taurate and plotted on the standard curve. The *in vitro* potency of the derivative was calculated as 833.3 µg mg^{-1}. The erythromycin base used that was 920 µg mg^{-1} which was the value of *in vitro* potency. The *in vitro* antimicrobial spectrum, by the two-fold agar dilution test [68] the minimum inhibitory concentration (MIC) of the derivative was determined. Brain heart infusion agar plates mixed with erythromycin base and its derivative were inoculated each with one loopful of 24 h old broth culture. The plates were incubated for 18 h at 37 °C and the MIC was calculated for the following organisms: *Staphylococcus aureus* NCIM 2079, *Klebsiella pneumoniae* NCIM 2957, *Bacillus pumilis* NCIM 2327, *Bacillus subtilis* NCIM 2063, *Escherichia coli* NCIM 2065 and *Pseudomonas aeruginosa* NCIM 2036. For release study using dialysis bag method erythromycin antibiotic was carried out. About 10 mg of EM-loaded LCS microcapsules were dispersed in 5 ml of phosphate buffer saline solution (PBS) at pH 7.4 and poured into a dialysis bag (MW cut off of 5 kDa). The dialysis bag was immersed in 50 ml of PBS receptor media with continuous stirring 100 rpm at 37 ± 0.4 °C. About 4 ml aliquot was withdrawn from the receptor media up to 48 h. An equivalent volume of a fresh PBS media was replenished into the receptor media. UV-Vis spectroscopy was used for the release sample analyzed at 330 nm and the amount was calculated by using the Erythromycin standard curve.

***In vivo studies*:**

According the ethical standards all the biological experiments are performed to determine i*n vivo* pharmacokinetics data by using Swiss albino male rabbits. Test animals 1.5 kg body mass and around of 6 months old are used in this study. The rabbits were fed fodder feed (standard pellets, Pranav Agro Industries, India), vegetables (carrot and cabbages) and the free access to water. The feed was maintained at 120 to 150 g per day per rabbit and also prevent obesity. Animals were kept separately in the cages. The average temperature of the animal house was maintained at 18 to 21 ºC throughout their life span. There were two experimental groups that is control and test, each consisting of 5 rabbits. The control group received 8 mg kg^{-1} body mass of erythromycin base and the experimental group received 8.3 mg kg^{-1} body mass of the derivative (equivalent to 8 mg kg^{-1} body mass of the base) by intravenous injection through marginal ear vein. The dose was equivalent to the 500 mg of erythromycin base dose administrated to a 60 kg human adult. Blood samples (0.5 ml) were taken firstly after the injection with a different time intervals for about three hours after injection. Serum was separated out from the each blood sample and the erythromycin concentration was determined in the serum by the microbiological assay [67]. The concentration of the Erythromycin was calculated in serum with the graphically from the standard curve plotted with the base obtained for this purpose using the single point assay [65].

Adult male albino rats weighing 110 to 130 g were obtained from the Laboratory Animal Center (Dokki, Giza, Egypt). All animals had a standard diet and water *ad libitum*. The rats were put in plastic cages in a well-ventilated room and the temperature 25 ± 3 °C for 2 weeks prior the start of experiment as an acclimatization period. EM-loaded LCS oral doses are administered. Rats were fasted overnight for 12 h with free access to water. The rats were received an oral dose (50 mg kg^{-1}) of EM-loaded LCS microcapsules suspension in 1 ml of pure water without constraining the animals. Oral administration was carried out with a rigid gavage tube. The rats were sacrificed *via* cervical decapitation. The blood samples were collected into heparinized 1.5 ml Eppendorf tubes at 0.5, 1, 2, 3, 5 and 6 h after the oral administration. Plasma samples were separated by centrifugation of the collected blood for 15 min at 3000 rpm and stored at -80 °C for subsequent analysis. The concentrations of EM plasma in rats were measured chromatographically using an HPLC, Agilent Technologies 1200 Series, and G1315D DAD (USA) with a Zorbax NH_2 Analytical 4.6 × 250 mm 5-micron column. The composition of mobile phase was constant (isocratic elution) containing (A: 10 % 10 mM dibasic hydrogen phosphate buffer, pH 6.5 and B: 90 % methanol). Erythromycin was measured flow rate 1.5 ml/min at 25 °C. The erythromycin was analyzed at the 210 nm wavelength by using the UV detector.

***Clinical Studies*:**

World Medical Association et.al in a two-year study (2011 to 2013), a total of 100 clinical and normal flora pneumococcal isolates (50 each) was collected from the hospitals and private clinical laboratories in Tehran and Iran. The different type of meningitis, pneumonia, or bacteremia were confirmed by the collected patients'

samples. None of the patients or healthily subjects received any forms of PCV. The normal flora isolates were collected from the healthy nasopharynx individuals who did not have any antibiotic treatments for at least 6 months preceding to the sampling and had no serious nasopharynx infections. According to the Declaration of Helsinki (1975) amended in 2013 [69]. The study was approved by the Ethics Committee of Iran University of Medical Sciences. For privacy reason, the identity of patients and clinical laboratories form whom/where the isolates had been collected remained anonymous throughout the study. A written consent, however, was obtained from the control volunteers. for species identification used the Standard microbiological techniques, including like hemolysis, Gram staining, bile solubility and susceptibility to optochin (1 µg) disc [70]. By the lytA and ply the identification of isolates was confirmed, genes using species-specific primers for polymerase chain reaction (PCR) [71]. Serotyping was performed using the Quellung reaction with antisera (Statens Serum Institut Copenhagen, Denmark).

Omar R. Sadeq, *et al*. carried out clinical studies on sixteen adult patients of mild acute bacterial pharyngitis, age ranged 22 to 65 years, with no earnest cardiovascular, hepatic, endocrine, renal or GIT pathologies, participated in this study, all patients gave written informed consent. In all subjects, complete blood count (CBC) and fasting glucose were measured before, upon completion of treatment, as well as, two weeks after discontinuation of erythromycin therapy. Mild acute bacterial pharyngitis in all patients was confirmed by a throat culture that revealed streptococcus pyogenes group A Streptococcus [GAS]) [72,73]. Patients were divided equally into two groups according to the gender; the first category includes eight male patients; five of them aged 50 to 65 years, the remaining are younger, aged 22 to 50 years. The second contains eight female patients; six among them aged 47 to 65 years, the other 2 patients of 22 years of age. All patients were medicated with erythromycin stearate 250 mg PO qid (orally four times a day) for 14 days. For a possible glycemic effect of erythromycin in a 4 week period, the subjects were investigated at the end of treatment, to ensure the efficacy of antibiotics and effect of the erythromycin on glucose levels is generally tested by the CBC and glycemic test.

Antoaneta Decheva, *et al*. carried out clinical studies, on tested 1862 clinical isolates of *S. pyogenes* which were recovered during the period 1995 to 2005 from patients with throat and skin infections. World Health Organization [74] recommended the isolates were identified by standard the methods. By the disk diffusion method following the criteria of NCCLS for erythromycin, clindamycin, tetracycline and chloramphenicol antibiotic susceptibility testing was performed [75]. Phenotypes of erythromycin resistance were defined by the double-disk diffusion test as described by Seppala, *et al*. [11]. We performed polymerase-chain reaction (PCR) for detection of the following genes: speA – encoding production of streptococcal pyrogenic exotoxin A; speF – encoding production of streptococcal pyrogenic exotoxin F; prtF1 – encoding production of protein F1. Primers and cycling parameters of the PCR have already been described by Bianco, *et al*. [76].

Hynes and Tagg, we tested the strains for proteinase production by a proteinase agar method described [77]. Johnson and Kaplan [78] describes the Production of serum-opacity factor was tested By a micro-technique with horse serum, emm sequence typing was performed on ABI 310 sequencing machine using the technique described on the following webpage of Centers of Disease Control and Prevention, Atlanta, GA, USA. In quantities of reaction mixtures and amplification cycling due to the different class of the machinery used where minimal modifications were applied. The statistical analysis was performed by $\chi 2$ test with Yates' correction for small numbers and with Fischer's ϕ transformation.

EXPERIMENTAL:

Erythromycin Tolerance Tested by Flow Cytometry (FCM):

Haihong Hao, *et al*. has shown the flow test of the Erythromycin i.e. procedure of concentration of bacteria was adjusted to a 0.5 McFarland density. Mueller Hinton broth Serial was prepared twofold dilutions of erythromycin. Erythromycin concentration ranged from 0.0625 to 8 µg/mL. A 100 µl aliquot of bacteria was added to 900 µl MH broth containing different concentrations of erythromycin and incubated at 42 ºC in a micro-aerobic condition for 3 h. Each and every firstly dilution was centrifuged and the supernatant discarded. Erythromycin treated bacterial cells and the pellet was washed twice with sterile PBS and propidium iodide (PI), a membrane-impermeable DNA-intercalating dye, was used to stain. One milliliter of buffer and 5 µL of PI were added to each sample, after that incubated for 30 min at 4ºC. FCM analysis was conducted on

CyAnADPTM FC500 flow cytometer with Summit TM software (Beckman Coulter, Miami, FL, USA). The intensity of fluorescence of 10,000 cells labeled with PI was analyzed to obtain the mean channel fluorescence (MCF).

RNA Extraction

Haihong Hao, *et al*. express the cells of ΦCj1199 or *C. jejuni* NCTC11168 were grown in Mueller Hinton agar plate under microaerophilic conditions for 24 h at 42 ºC. For the extraction of RNA, RNA protects Bacteria Reagent (Qiagen, Valencia, CA, and USA) was added to the cultures immediately after the incubation to stabilize mRNA. The total RNA from each sample was extracted using the RNeasy Protect Mini Kit (Qiagen, Valencia, CA, and USA) following the manufacture's protocol. The samples of RNA were extracted by four experiments freely.

DNA Microarray and Data Analysis

Haihong Hao, *et al*. has shown, By the DNA microarray the differential gene expression between ΦCj1199 and *C. jejuni* NCTC11168 was identified, which was supplied by Capital Bio Corporation (Santa Clara, CA, USA). For the synthesis of cDNA from an RNA template via reverse transcription, iScriptcDNA synthesis kit (Bio-Rad, Hercules, CA, USA) was used. The cDNA was labeled with Cy5 or Cy3dye. The labeled cDNA probes were co-hybridized onto one microarray slide (Roche NimbleGen 4×72K, Indianapolis, IN, USA).

By using of NimbleGen MS200 the hybridized slides were scanned, and the fluorescence intensities were collected with NimbleGen Scan Software, Linear normalization method was used which was based on expression of the housekeeping genes for data analysis. Normalized data was log transformed and loaded into MANOVA under Re-environment. Microarray spots with false discovery rate (FDR)-corrected dq-values<0.01and fold change≥2in the T-test were regarded as differentially expressed genes. On the basis of the genomic annotation in NCBI, differentially expressed genes were classified and then subjected to KEGG database for pathway analysis.

Drug Interaction:

Erythromycin is a potent inhibitor of the 3A isoform subfamily of CYP3A. Several reports and controlled studies have shown that erythromycin may interact with theophylline, carbamazepine, cyclosporin, tacrolimus, warfarin, digoxin, terfenadine, astemazole, cisapride, lovastatin, triazolam, and disopyramide [9,79,80] more than 700 drugs interact with erythromycin. Erythromycin is the prototype of macrolides that binds irreversibly on the 50S subunit of the bacterial ribosome, consequently inhibiting translocation step in protein synthesis, the effect depending on the concentration and on type of microorganisms.

Its activity is enhanced at alkaline pH; its action may be bactericidal or bacteriostatic. It should not be co-administered with lincomycin, clindamycin or chloramphenicol, because of pharmacodynamics antagonism, on 50S subunit [81,82]. In the antibacterial effect, erythromycin has different immune modulatory, anti-inflammatory and prokinetic activity, the exact underlying mechanism is not known, but possibly by decreasing the oxidative production of cytokines by neutrophils (IL-1, IL-6, IL-8 and TNF), in addition, production of IL-10 and platelet count are increased, the prokinetic activity of erythromycin refers to its ability to stimulate the release of motilin from endocrine M cells of enterocytes, and consequently sometimes erythromycin is employed for management of gastroparesis [83-86].

Orally administered erythromycin ethyl succinate is readily and reliably absorbed, it is widely distributed into most body compartments, with a little amount in the cerebrospinal fluid (CSF) that is increased in state of meningitis.

CONCLUSION:

It shows the continuous increase of the resistant bacterial strain causes a significant problem in the modern healthcare system and drug discovery. Erythromycin plays an important role as an antibiotic in recent and modern health care unit. It is first macrolide antibiotic drug and is further developed in to semisynthetic macrolides which are also introduced in the medical practice such as spiramycin, clarithromycin, josamycin and azithromycin, significantly changed anti-infective drug picture of 20th century. Although erythromycinis a potent Prokinetic but limited data exist concerning its efficacy in treating gastroparesis. Small sample sizes, uncontrolled designs, short duration, and inadequate symptom assessment limit available studies. Whilst there is considerable evidence to suggest that erythromycin may be a useful prokinetic agent in patients, the quality of these data is significantly limited by the lack of randomized placebo-controlled trials.

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