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**ORIGINAL ARTICLE**

# Investigation of RFID tag readability for pharmaceutical products at item level

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**Abstract**

*Background*: The applications of radio frequency identification (RFID) technology carry a tremendous potential for pharmaceutical industry. There is a pressing need to analyze the performance of RFID tags attached to various pharmaceutical dosage forms. *Method*: The readability of RFID-tagged pharmaceutical products is, for the first time, systematically investigated by experiments. Factors considered include dosage forms, ion concentration in solution, angle of rotation, and distance between the RFID tag and the interrogator. *Results*: Compared with empty container, the filling of any representative dosage forms causes deteriorated readability for the tag attached to container. Analysis of variance reveals that the effects of dosage forms, angle of rotation, and their interaction are statistically significant. In addition, an increase in distance (equivalent to higher RF attenuation level) and higher ion concentration in solution beyond a certain level have detrimental effect on tag readability. *Conclusion*: The analysis shows that the RFID tag readability is strongly dependent on the factors that are experimented with. The level of the factors for optimum RFID system performance should be adjusted based on the particular application.

**Key words:** *Angle of rotation; attenuation; item-level packaging; pharmaceutical dosage form; RFID; tag readability*

## Introduction

The pharmaceutical industry is a gigantic industry. In 2007, the global sales totaled 712 billion USD. Figure 1 shows the annual global sales of the pharmaceutical industry for the period 2000–2007. United States is the biggest market for the pharmaceutical industry. The sales reached 286.5 billion USD in the United States in 2007[1] and it constitutes approximately 40% of the total global market. Europe, Japan, and Latin America are the next biggest markets constituting around 31.1%, 8.8%, and 4.8% of the total global market, respectively[2].

Two readily available technologies that can be used for tracking and tracing the pharmaceutical products are the barcode technology and the promising radio frequency identification (RFID) technology[3]. A barcode is a machine-readable representation of the information in a visual format on a surface. It can be read by optical scanners called barcode readers or other similar devices. On the contrary, RFID technology features the tags that store the item information. The RFID interrogators capture the item information from tags and pass them through the middleware to the enterprise applications. Barcode technology requires line of sight for the retrieval of the information. In this regard, RFID technology has a distinct advantage over barcode technology and retrieves the information through wireless communication without the line-of-sight requirement. Another advantage of RFID technology is that the tags can be read simultaneously by one interrogator, whereas barcode technology necessitates the sequential scanning of the barcodes, which impedes the efficiency of tracking and tracing system[4]. Note that RFID systems can be based on active and passive RFID technologies. Active RFID tags have an onboard battery, whereas passive tags do not. The discussion of this article is limited to the latter type in that the cost of a passive tag is merely a fraction of that of an active tag.

The frequency of the RFID system determines the key characteristics of the performance in applications. For the retailing and defense industries, ultra-high

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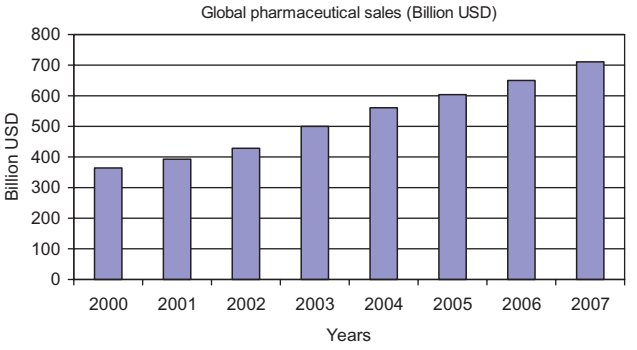


**Figure 1.** Global pharmaceutical products market (Source: IMS Health—Global Sales and Prescription Information—2007).

frequency (UHF) is becoming a norm especially in the pallet-level tagging. Wal-Mart mandates the suppliers to provide RFID tags on their shipments, and most of the tags utilized for this purpose are UHF Generation 2 tags. For the pharmaceutical industry, however, there is no single answer for which frequency RFID systems should be operating at. Although the 2004 FDA report recommends using high-frequency (HF) tags in the item-level package and UHF tags for the cases and pallets[5], successful implementations of both UHF and HF systems for item-level packaging have been reported[6–8]. Both UHF and HF systems have their pros and cons. Typically, UHF systems operate at 902–928 MHz frequency, whereas HF systems use 13.56 MHz band. In general, UHF systems have faster read rate, longer read range, and lower tag cost[9,10]. Nevertheless, the tags using UHF frequency have noticeable performance problems whenever operating in the vicinity of metal objects and liquid[11]. Forms of pharmaceutical packaging include bottles, vials, syringes, tubes, and blister packs. Many of them are metal foil sealed and/or have liquid content. It causes a major difficulty for the implementation of UHF RFID systems for pharmaceutical products at item level.

Another concern associated with the frequency is the thermal effect. It is believed that the RF power might change the temperature of the pharmaceutical product that the tag is attached to. Especially, the tags operating at UHF or microwave frequency are more likely to have the thermal effect. In some instances, the rise of the temperature of the pharmaceutical product might affect the efficacy, purity, or safety of the product. Currently, FDA is investigating the effect of RFID tags on the integrity of the particular biological products that have unstable protein structures. In a study, various drug formulations are exposed to 915 MHz electromagnetic signal with the electromagnetic source located 20 cm away from the product. After 7 hours of continuous exposure, the average temperature of the product rises by only 0.3°C, which is considered to be within the acceptable level[12].

In general, for minimum operational complexity and cost, it is desirable to use a single type of RFID tag that can be universally attached to different forms of pharmaceutical product. Tailored tag designs for specific pharmaceutical products should provide optimal performance, but it is not very practical at this stage. Up to date, pharmaceutical item-level tagging is still at its infancy period, whereas the interest has been growing. Pharmaceutical companies in partnership with RFID system manufacturers are conducting research and join the bandwagon by implementing their solutions. The most notable adopters who have success in implementing this technology for pharmaceutical products are Pfizer and Purdue Pharmaceutical[13]. Meanwhile, RFID technology carries a huge potential for improving the healthcare systems. A recent study indicates that the global market for RFID tags and systems in healthcare systems will grow from 90 million USD in 2006 to 2.1 billion USD in 2016[14]. However, the adoption of RFID technology by pharmaceutical industry is slower than expected because of various reasons such as costs, IT complexity, component performance, read accuracy, and installation.

There are very few articles that discuss the application of RFID technology for manufacture and distribution of pharmaceutical products in the literature. Sabogal and Tholke[15] provide a guideline on the integration of RFID technology with the SAP ERP system for manufacture of pharmaceutical products. Connolly[16] discusses about the RFID tags that might be used during packaging and processing of foods and pharmaceuticals. Lawson and Kedward[17] provide information on current legislations and the future pedigree requirements imposed on the pharmaceutical industry. Adams and Burke[13] discuss about how RFID system might be incorporated in the filtration phase of the pharmaceutical product manufacturing. However, to the best of the authors' knowledge, there were no articles investigating RFID tag readability for pharmaceutical industry in the literature as of the time this article was written.

Several critical factors play an essential role in successfully implementing RFID technology for item-level pharmaceutical products. One is that within a pharmaceutical container, there might be a variety of pharmaceutical products with different dosage forms such as tablets, powders, creams, and solutions. Each dosage form is composed of raw materials of different physical forms such as active ingredients, inactive ingredients, and the base materials, which are the major constituents of pharmaceutical products in terms of weight. Therefore, it is important to evaluate the impact of the pharmaceutical dosage form on RFID system performance. For solutions, it will be helpful to know how the RFID performance responds to the change in ion concentration. The other is that

orientation and read distance of RFID tags with respect to the interrogator are two important criteria for deploying RFID systems. They should always be set in a proper way to ensure the smooth exchange of the RF signals. Hand-held and vehicle-mount interrogators can effectively address the orientation issue because they integrate the antenna and interrogator in one device and are portable. However, for RFID systems that employ fixed mount interrogators, effective reading of RF signals depends on how the tags are oriented with respect to the interrogators. In addition, good orientation and appropriate distance help configure the position of the fixed-mount interrogator antenna in the moving conveyor and set up the right position of the products in the packaging. Read range is an important factor for an RFID system. It reflects the ability of transmitting and receiving the signals between the tag and the interrogator with respect to the distance between them. It is common for users and RFID manufacturers to push for long read-range tags and interrogators. Sometimes, for the item-level RFID tagging, this might not be the best approach. For example, there might be a necessity for the read distance to be limited to avoid the interference with RFID interrogators operating in the same environment.

To bridge the research gap, a comprehensive study is called for on the readability of RFID tags applied at item-level pharmaceutical containers. The study aims to investigate how the following factors affect the RFID tag performance in item-level tagging: (1) the pharmaceutical dosage forms, (2) the angle of rotation and distance of the tag with respect to the interrogator, and (3) the ion concentration of pharmaceutical solutions. For each factor, a statistical hypothesis testing is performed. The null hypothesis here is that the factor, for example, the dosage form, does not have significant effect on the readability. Correspondingly, the alternative hypothesis is that the factor has significant effect on the readability performance. Furthermore, if the hypothesis test shows that a factor does have a significant effect, the corresponding effect at each factor level is analyzed. For instance, as it will be shown later, the dosage form significantly affects the readability. Thus the effect of each dosage form, including tablets, powder, cream, and solutions, is further analyzed.

With an accurate understanding of the performance of RFID tags with respect to these factors, the pharmaceutical manufacturers will be more confident in selecting and implementing the RFID technology for tracking and tracing purposes. The findings of this study might also be used for designing and developing RFID tags for a specific dosage form. In addition, we believe that this study can shed light on the research about other potential applications of RFID technology for pharmaceutical products, such as the design of tamper-proof container.

## Materials and methods

The experiments are conducted in a laboratory with the ordinary room settings. An anechoic chamber is regarded as not necessary and also not desired for the following two reasons. Most importantly, in the tests, the tags are always kept close in the area close to near field of the RFID antenna. This resembles the setup of RFID devices on pharmaceutical packaging line, and the short distance can reduce the noise effects from the environment. On the contrary, in the actual production environment, there are various sources of electromagnetic noise, such as moving machinery, sensors, and computers. Also, there are objects that might absorb or reflect the RF signals such as the metallic parts in conveyor belt, operators running the machinery. The laboratory environment in this study contains the aforementioned noise sources and thus can more or less simulate the operating conditions in real-life settings in case that the RF signal interference needs to be considered. In this regard, the results from the laboratory environment should provide more insightful information than those from the anechoic chamber.

Four major sets of experiments are conducted in this study. These are rotation test in *XY*-plane, rotation test in *XZ*-plane, power attenuation test, and ionization impact test. Rotation test in *YZ*-plane is deemed to be unnecessary. As the tag is on *YZ*-plane, conducting rotation test would merely mean rotating the tag around the *X*-axis without changing the distance between the tag surface and the antenna. *XZ*- and *XY*-plane tests cover the scenario of the spatial displacement as well as the rotational displacement.

### *Selection of dosage forms*

There are several criteria for selecting the pharmaceutical products for the experimentation. Base material deserves consideration because it accounts for the majority of the pharmaceutical product's weight (up to 99%). Another selection criterion is the popularity of the pharmaceutical product in the market. Pharmaceutical products with large market demand have high priority for being experimented with. In this study, tablets (coated and uncoated), powder, cream, solutions, and purified water are selected for comparing the performance of RFID tags on pharmaceutical products. Table 1 lists the pharmaceutical products' names used for the experiments.

The empty pharmaceutical container is included in the experiment even though it is not a real pharmaceutical dosage form. The empty container serves as a control group in this case. It should provide a near-to-ideal situation for RFID tagging because of the lack of pharmaceutical product that might otherwise impede the tag performance. If the results are different between a

**Table 1.** Pharmaceutical product dosage form information.

| Dosage form | Brand name | Product type | Major base material |
|---|---|---|---|
| Tablets | Select Brand™ | Aspirin | Cellulose |
| Tablets (coated) | Equate Enteric™ | Coated aspirin | Starch, talc |
| Powder | Johnson-Johnson™ | Baby powder | Talc |
| Cream | Palmer's Cocoa Butter Formula™ | Concentrated cream | Petrolatum |
| Solution 1 | Non-drowsy Daytime™ | Cold/flu relief | Glycerin |
| Solution 2 | Listerine™ | Mouth wash | Alcohol |
| Purified water | Aquafina™ | Purified water | De-ionized water |

container filled with pharmaceutical products and the empty container, the presence of the pharmaceutical product is considered to affect the tag and interrogator communication. For all the pharmaceutical products selected, the same type of plastic prescription container in dark orange color is used to maintain consistency. The container is cylindrical in shape and has a diameter of 50 mm and a height of 75 mm.

### *Equipment*

The experiments utilize RFID tags, an RFID interrogator with antenna, the software needed for retrieving the data from the interrogator and for analysis, and the equipment used for fixing and adjusting the angle of rotation of the pharmaceutical product container with respect to the interrogator antenna. Impinj Satellite™ UHF Generation 2 tags are chosen and attached to the containers. This tag is specifically designed for pharmaceutical item-level tagging—its antenna design utilizes a loop/dipole hybrid configuration, which contributes to the tag readability both in near and far field.

The interrogator used in the experiments is Alien ALR-9780 UHF RFID reader, with the capability of connecting to four different antennas simultaneously. One circularly polarized antenna is used with the interrogator using the RS-232 serial port. To ease the data read and export process, a separate Microsoft Visual Basic™ application programming interface (API) module is written to connect the interrogator to a personal computer, and to export the data to Microsoft Excel™ data file directly. The picture of the components of RFID system (i.e., interrogator, antenna, and tags) and the pharmaceutical containers filled with pharmaceutical products are shown in Figure 2A and B, respectively.

### *Setup of rotation tests*

The schematic of the relative rotation of the tagged pharmaceutical container and the antenna along with the

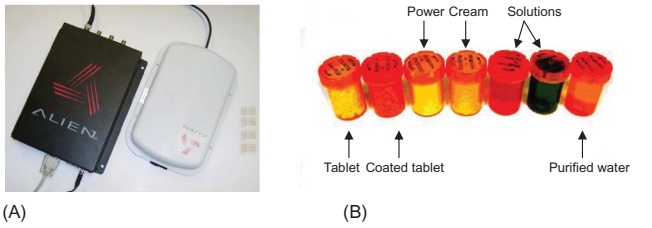


**Figure 2.** Hardware and materials used in the experiment. (A) Alien RFID interrogator and antenna, and Impinj tags; (B) seven pharmaceutical dosage forms.

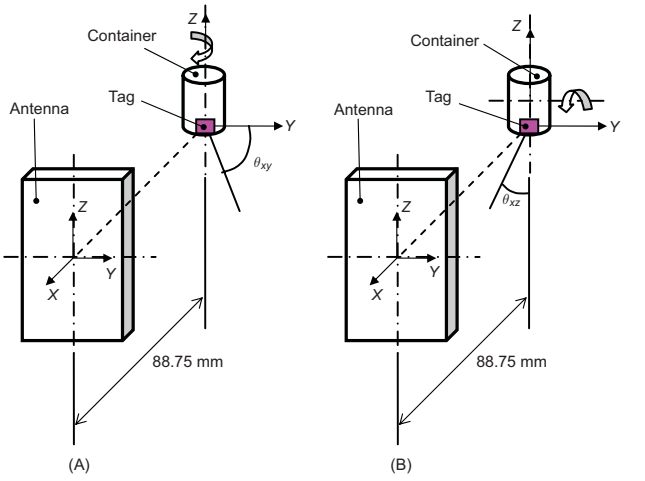


**Figure 3.** Schematics of experimental set-up. (A) Rotation test in *XY*-plane; (B) rotation test in *XZ*-plane.

coordinate axis are provided in Figure 3A and B. The Impinj Satellite™ RFID tag is attached to the side wall of the cylindrical container. Initially, the RFID tag is adjusted to be at the same height with the middle ridge of the interrogator antenna. During the experiments, the distance of the central axle of the container to the interrogator antenna is fixed to 88.75 mm for both *XY*-plane and *XZ*-plane rotation tests. In *XY*-plane rotation test, the closest distance of the tag to the interrogator antenna is approximately 63.35 mm at 0°, and the furthest distance is 114.15 mm at 180°. In *XZ*-plane rotation test, the closest distance of the tag to interrogator antenna is approximately 50 mm at 90° and the furthest distance is 126.75 mm at 270°. This is believed to be a reflection of the normal conditions in real-life applications of item-level tagging in the pharmaceutical manufacturing floor, where the pharmaceutical products are transferred from one location to another mostly by conveyor belts, around which fixed RFID antennas can be mounted. For instance, during the transfer, these pharmaceutical containers might roll around its axis, which causes changes in rotation angles of the RFID tag with respect to the interrogator.

For each dosage form, 12 levels of angles of rotation are tested both for the *XZ*-plane and the *XY*-plane from

**Table 2.** Factors and levels for design of rotation tests.

| Factors | Levels |
|---|---|
| Dosage form | Empty container, tablet, coated tablet, cream, powder, solution 1, purified water |
| Degree of rotation | 0°, 30°, 60°, 90°, 120°, 150°, 180°, 210°, 240°, 270°, 300°, 330° |

0° to 330° that are spaced equally 30° apart. For the rotation tests in *XY*-plane, the *XZ*-plane rotation angle is fixed at 0°, and for the rotation test in *XZ*-plane, the *XY*-plane rotation angle is fixed at 0°. As such, there are two factors that are included in each rotation test, and Table 2 summarizes the levels of these factors in the experimental design. During tests, the RFID interrogator is set to send 255 interrogation RF attempts in each read cycle to the RFID tag. The signals reflected by the tag and received by the interrogator are considered to be successful reads. The response rate is defined as the ratio of number of successful reads to the number of interrogation attempts,

$$\text{Response rate} = \frac{\text{number of successful reads}}{\text{number of interrogation attempts}},$$

and this measure is calculated for each cycle. To obtain adequate number of data points for ensuring the statistical significance, the read cycle is repeated for 500 times for each combination of dosage form and angle of rotation, and the mean response rate is calculated out of these 500 repetitions for each case in both *XY*-plane and *XZ*-plane rotation tests. On the average, one read cycle takes 1 second.

### *Attenuation and ionic impact tests*

The purpose of power attenuation test is to measure the effect of the distance between the interrogator antenna and the tag on the response rate for the pharmaceutical products. In the test, the rotation angles in *XY*- and *XZ*-plane are fixed. Rather than varying the distance between the interrogator and the tag, we take another approach for the same purpose. Our approach is based on the classical Friis equation, which posits that the change in the distance can be simulated by adjusting the attenuation level of RF signal[18]. The Friis equation is given as follows:

$$r = \frac{\lambda}{4\pi}\sqrt{\frac{P_t g_t g_r}{P_r}},$$

where $P_r$ is the interrogator transmitting power, $P_t$ is the tag receiving power, $g_r$ is the interrogator transmitting gain, $g_t$ is the tag receiving gain, $\lambda$ is the wave length, and $r$ is the distance between interrogator antenna and tag antenna. Some researchers have adopted this approach as well. For instance, Ramakrishnan adjusts the attenuation of RF signals to simulate the distance effect on the performance of various UHF RFID tags[19]. In line with Friis equation and existing work done in this field, we keep the distance between the tag and the interrogator fixed and simulate the change in distance by adjusting signal power attenuation for the interrogator antenna. The attenuation can be set anywhere between 0 and 16 dB, which is the maximum allowable in the device setting of the RFID interrogator. Similar to rotation tests, at each attenuation level, the transmitting and receiving cycle is replicated for 500 times.

As mentioned previously, the purpose of the ionization impact test is to investigate the effect of ion concentration in solution on RFID response rate. Similarly, the rotation angles in *XY*- and *XZ*-plane are fixed. The experiment starts with adding 100 mg of table salt (i.e., sodium chloride) to 67 mL of Listerine™, and the response rate is measured. This step is repeated in succession till no signal is received by the interrogator (i.e., the response rate drops to 0%). It is shown that the response rate drops to 0%, after the inclusion of 900 mg of table salt to Listerine™.

## Results and discussion

### *Rotation tests*

Figure 4A–G depicts the response rate of different dosage forms with respect to angle of rotation in *XY*-plane in radar charts. Clearly, each dosage form has unique pattern in response to the change of rotation angle, and overall the response is anisotropic and not uniform. The best performance is obtained with empty container, which indicates that all the dosage forms have detrimental effect on the readability of RFID tags. Moreover, by comparing Figure 4B–D, one can see that regardless of the difference in base materials and existence of coating, tablet has similar performance as coated tablet; the powder form exhibits a significant drop in the readability. Another interesting observation is very poor reading rates regarding Solution 1 as depicted in Figure 4F. Solution 1 is the multisymptom cold and flu relief solution, which is widely used as the counter medicine for fighting against these ailments. The tags attached to the containers having this dosage form significantly lag behind other dosage forms in terms of response rate in the *XY*-plane rotation tests. It is speculated that the reasons could be the contents of this pharmaceutical product, and potential ion effects in the solution.

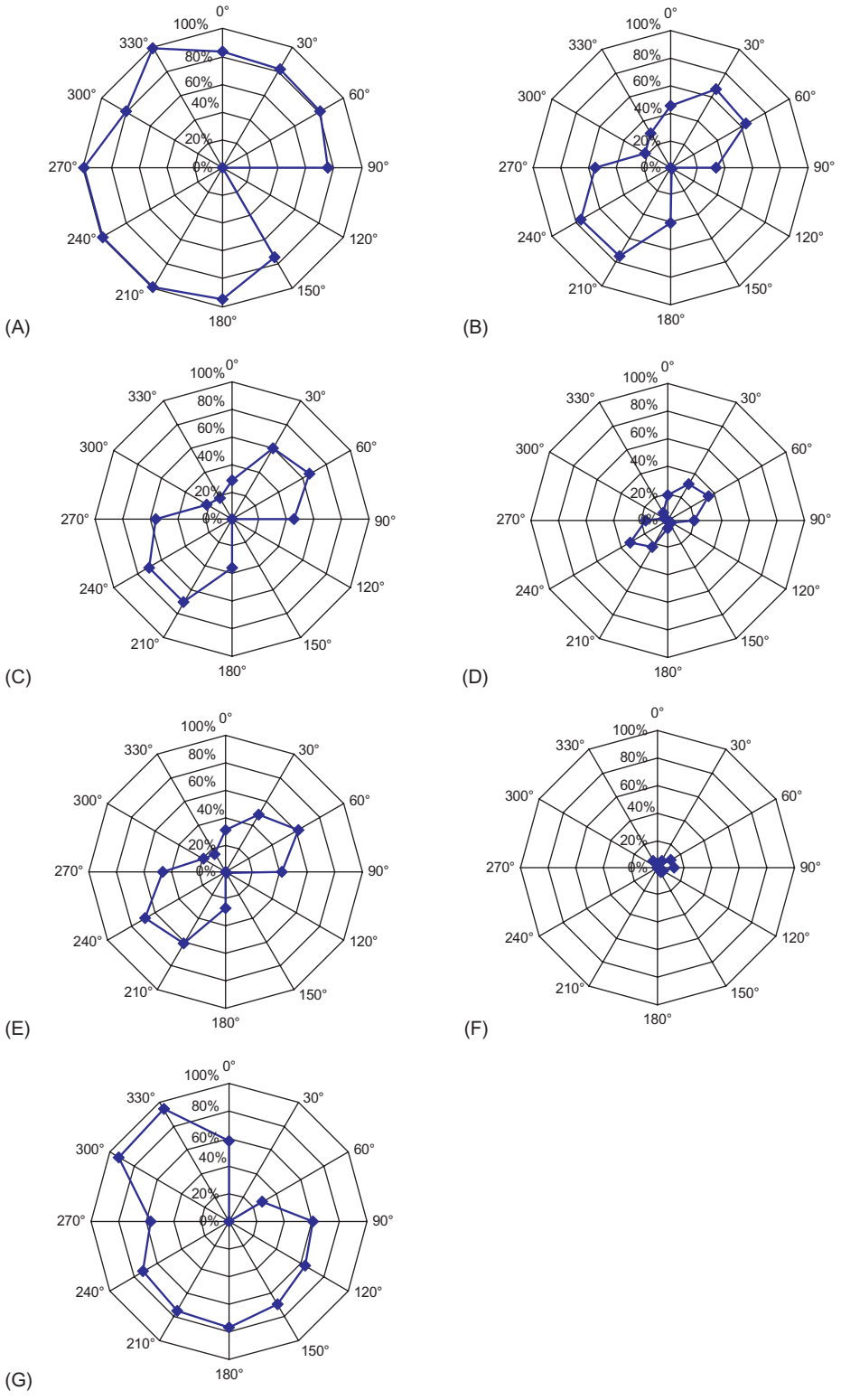


**Figure 4.** Radar charts of RFID response rate in *XY*-plane for, (A) empty container, (B) tablet, (C) coated tablet, (D) powder, (E) cream, (F) Solution 1, (G) purified water.

The rotation of containers in *XY*-plane is more important in the pharmaceutical bottling and packaging line. The actual rotation in *XZ*-plane is not very common, but it does occur in some occasions. Same approach is followed as in the case of rotation tests in the *XY*-plane. Two-factor full-factorial design is chosen, and the corresponding analysis of variance (ANOVA) is conducted. Figure 5A–G depicts the response rate of different dosage forms with respect to angle of rotation in *XZ*-plane in radar charts. Similar to the results of *XY*-plane test, different response patterns can be observed for different dosage forms. The best performance is obtained with empty container, whereas the worst performance is obtained with Solution 1. The detrimental effect of pharmaceutical dosage form is confirmed one more time. In addition, the inferior performance of powder form as compared with tablets is also observed.

**ANOVA of rotation effects in *XY*-plane**

The statistical tests on the experimental data are conducted using Minitab software package. ANOVA is employed to compare the mean values of each combination of dosage form and rotation in *XY*- and *XZ*-plane. The observations in a factorial experiment $y_{ijk}$ can be described by the effect model that is represented below:

$$y_{ijk} = \mu + \tau_i + \beta_j + (\tau\beta)_{ij} + \varepsilon_{ijk} \begin{cases} i = 1,2,\ldots,7 \\ j = 1,2,\ldots,12 \\ k = 1,2,\ldots,500 \end{cases},$$

where $\mu$ is the overall mean effect; $\tau_i$ is the effect of the *i*th level of the row factor, which represents the *i*th type of the dosage form; $\beta_j$ is the *j*th level of the column factor, which represents the *j*th level of angle of rotation; $(\tau\beta)_{ij}$ represents the interaction effect between the dosage type and the angle of rotation; $\varepsilon_{ijk}$ is the random error component; and index *k* denotes the replications for each level of dosage form/angle of rotation pair. We employ a fixed-effects ANOVA model for analyzing the statistical significance of individual factors. The statistical significance of the effect of a specific factor or an interaction is determined by the amount of deviation from the overall mean response rate that can be attributable to that specific factor or interaction.

After constructing the statistical design, we conduct a full-factorial ANOVA. The factors incorporated in ANOVA model are (1) pharmaceutical dosage form and (2) angle of rotation. Our goal for conducting this analysis is to identify the effects of angle of rotation along *XY*-plane and pharmaceutical dosage form on the response rate. Table 3 summarizes the Minitab output for the two-factor full-factorial experimental design on *XY*-plane rotation test. Based on the individual and overall *F* values of the model and the corresponding probabilities, it is apparent that the dosage form, the angle of rotation, and the interaction effects are significant. However, for a specific dosage form, there might be the cases in which angles of rotation yield similar response rates that are not statistically different from each other. Similarly, for a specific angle of rotation, there might be the cases in which dosage forms yield similar response rates that are not statistically different from each other. To find out these relations, we also employ the one-way ANOVA tests.

In order for ANOVA to be valid, the residuals need to be normally and independently distributed with zero mean and constant variance. The normality assumption can be checked with the normality plot shown in Figure 6. It reveals that overall residuals are indeed normally distributed. The independence assumption can be checked using residual of response rate versus replications, which is shown in Figure 7. It can be seen that there is no obvious visible pattern in the residuals with respect to replications, which indicates that the residuals are independently distributed and the error terms are not correlated among each other or with the angle of rotation and the pharmaceutical dosage form. The homogeneity assumption can be checked using the residuals of response rate versus the dosage form and angle of rotation as shown by Figures 8 and 9. Both figures indicate that the residuals are not dependent on a specific angle of rotation or dosage form. One can also observe that, for empty container and Solution 1, the residuals are not lined up symmetrically along the line of residual = 0 and the same is true for angles of rotation of 210° and 240°. However, the overall degree of asymmetry deviations is not severe. In addition, our two-factor full-factorial analysis has a balanced design, which is more robust to the violation of homogeneity assumption compared with unbalanced ANOVA. Therefore, we conclude that homogeneity assumption also holds true.

By examining one-way ANOVA results, we can group the similar dosage forms for specific angle of rotation in *XY*-plane. For grouping purposes, we use the Tukey's test with a confidence interval of 95%. Table 4 summarizes this relation. The '&' sign indicates that the mean response rates of the dosage forms connected by this sign are not statistically different. Note that a specific dosage form might be included in different groups. Similar analysis is performed for grouping of angle of rotation for specific dosage form by conducting one-way ANOVA and employing Tukey's test using 95% confidence interval. The results are summarized in Table 5. The grouping results are helpful to the design of RFID tags for a specific dosage form as well as the deployment of RFID devices in the pharmaceutical manufacturing floor.

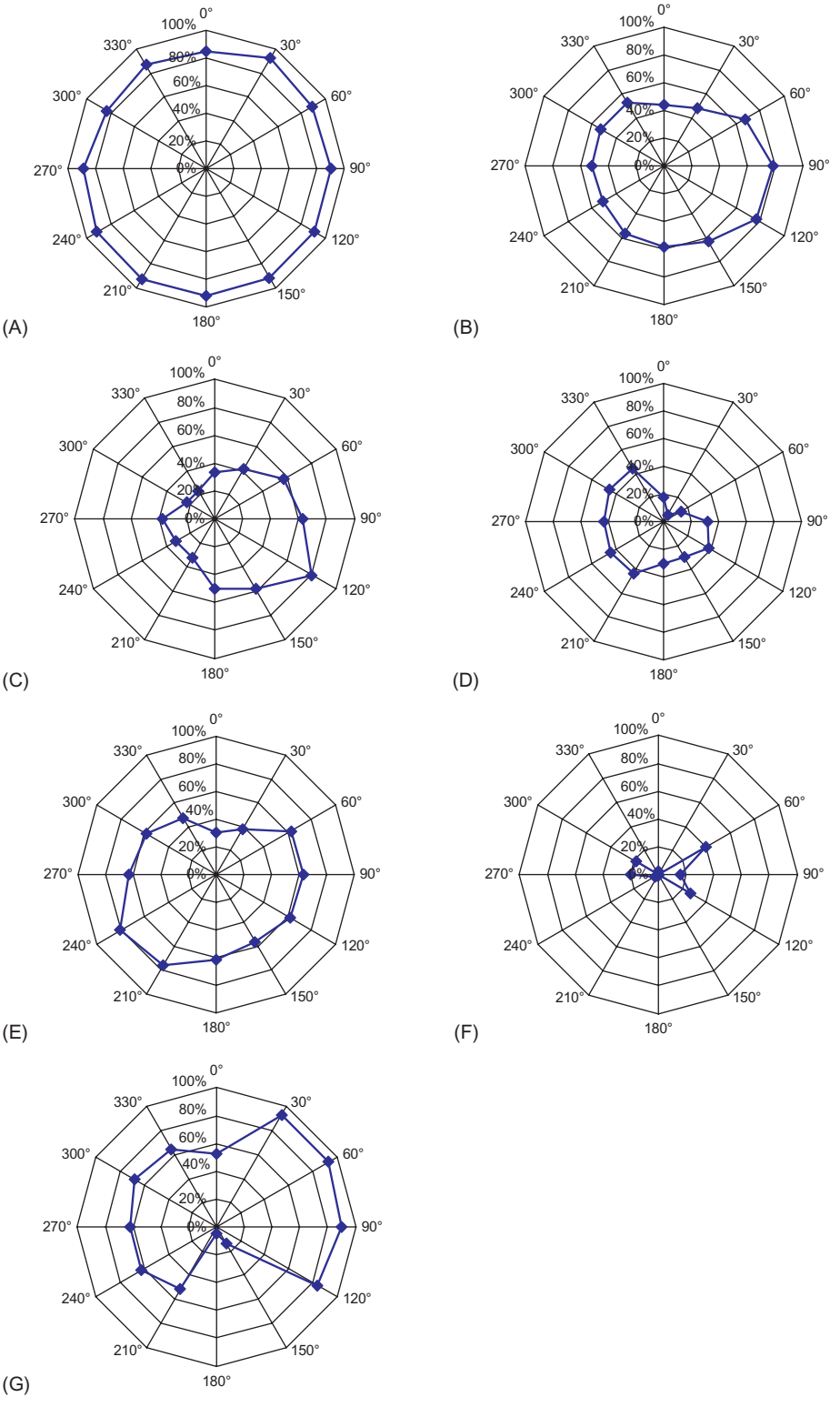


**Figure 5.** Radar charts of RFID response rate in *XZ*-plane for, (A) empty container, (B) tablet, (C) coated tablet, (D) powder, (E) cream, (F) Solution 1, (G) purified water.

**Table 3.** Two-factor ANOVA results for rotation tests in the *XY*-plane.

| Source | DF | Sum of squares | Mean square | *F* value | *Pr* > *F* |
|---|---|---|---|---|---|
| Dosage_Form | 6 | 2082.10 | 347.02 | 3916.61 | <0.0005 |
| Rotation | 11 | 1017.22 | 92.48 | 1043.71 | <0.0005 |
| Dosage_Form × rotation | 66 | 1284.98 | 19.47 | 219.74 | <0.0005 |
| Error | 41,916 | 3713.81 | 0.0886 | | |
| Corrected total | 41,999 | 8098.11 | | | |
| $R^2$ | Coeff var | Root MSE | Response rate mean | | |
| 0.5414 | 102.49 | 0.2977 | 0.45004 | | |

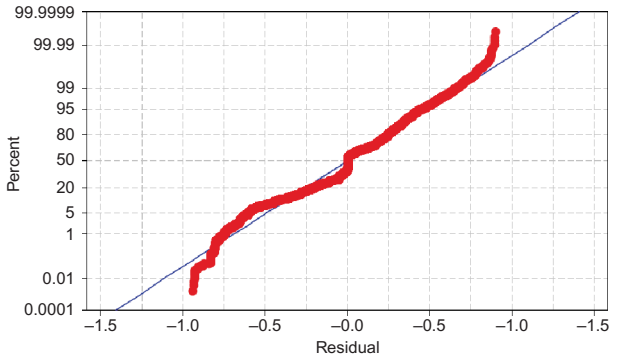


**Figure 6.** Normal probability plot of residuals for the rotation test in *XY*-plane.

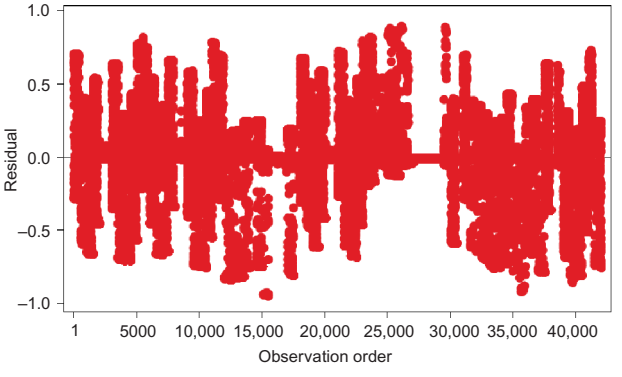


**Figure 7.** Residuals versus observation order for the rotation test in *XY*-plane.

## ANOVA of rotation effects in *XZ*-plane

Table 6 summarizes the results of ANOVA. Similar to the case in *XY*-plane rotation tests, the model shows that the treatment effects (i.e., dosage form and angle of rotation) as well as interaction effect between these two factors are statistically significant based on the individual and overall *F* values. To understand which of the dosage forms and angles of rotation have response rates significantly different than others, one-way ANOVA tests are performed. We conduct the same analysis as for the case of *XY*-plane rotation tests to check the validity of the ANOVA. Similar results are obtained and the ANOVA model is proven to be valid. For the sake of brevity, the details of the one-way ANOVA results are not listed.

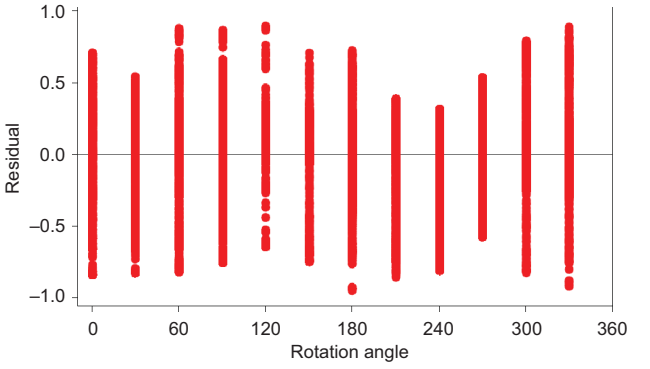


**Figure 8.** Residuals versus angle of rotation for the rotation test in *XY*-plane.

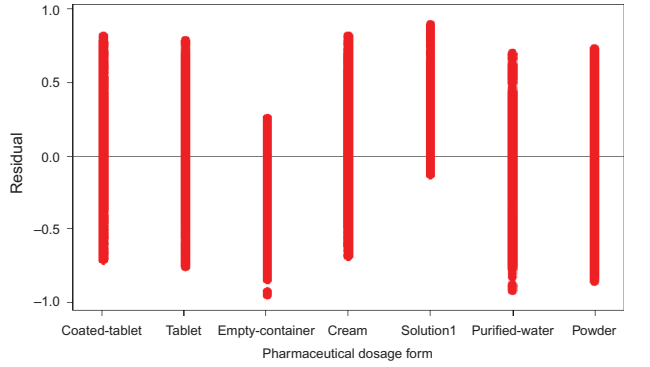


**Figure 9.** Residuals versus pharmaceutical dosage form for the rotation test in *XY*-plane.

**Table 4.** Grouping with respect to response rate among pharmaceutical dosage forms for a specific degree of rotation in *XY*-plane.

| Degree of rotation | Dosage form grouping with respect to response rate |
|---|---|
| 0° | Coated tablet & cream |
| 30° | Purified water & solution 1 |
| 60° | Coated tablet & cream & tablet, purified water & powder |
| 90° | Coated tablet & cream |
| 120° | Coated tablet & cream & empty container & tablet & powder |
| 150° | Coated tablet & cream & tablet & solution 1 & powder |
| 180° | None |
| 210° | Coated tablet & tablet & purified water |
| 240° | Coated tablet & cream & purified water, coated tablet & tablet & purified water |
| 270° | Coated tablet & tablet & powder & purified water |
| 300° | Coated tablet & cream & tablet, coated tablet & tablet, powder & solution 1 |
| 330° | Coated tablet & cream, powder & solution 1 |

**Table 5.** Grouping with respect to response rate among degree of rotation for a specific dosage form in *XY*-plane.

| Dosage form | Angle of rotation grouping with respect to response rate |
|---|---|
| Empty container | 0° & 30° & 60° & 300°, 90° & 150°, 90° & 300°, 180° & 210° & 240° & 270° & 330° |
| Tablet | 0° & 180°, 30° & 60°, 90° & 330°, 120° & 150°, 120° & 150°, 210° & 240° |
| Coated tablet | 30° & 60°, 30° & 270°, 60° & 210° & 240°, 120° & 150°, 300° & 330° |
| Cream | 0° & 180°, 30° & 270°, 60° & 210°, 60° & 240°, 90° & 270°, 120° & 150°, 300° & 330° |
| Powder | 0° & 90°, 30° & 60 & 240°, 120° & 150° & 300°, 120° & 180°, 0° & 210°, 180° & 330° |
| Solution 1 | 0° & 30° & 90°, 0° & 30° & 330°, 30° & 180° & 330°, 180° & 270°, 210° & 240° |
| Purified water | 0° & 90° & 120°, 0° & 90° & 270°, 120° & 150°, 150° & 210° & 240°, 180° & 210° & 240°, 300° & 330° |

**Table 6.** Two-factor ANOVA results for rotation tests in the *XZ*-plane.

| Source | DF | Sum of squares | Mean square | *F* value | *Pr* > *F* |
|---|---|---|---|---|---|
| Dosage_Form | 6 | 2500.42 | 416.74 | 4636.47 | <0.0005 |
| Rotation | 11 | 417.30 | 37.94 | 422.07 | <0.0005 |
| Dosage_Form* rotation | 66 | 1081.25 | 16.38 | 182.27 | <0.0005 |
| Error | 41,916 | 3767.50 | 0.0899 | | |
| Corrected total | 41,999 | 7766.48 | | | |
| $R^2$ | Coeff var | Root MSE | Response rate mean | | |
| 0.5149 | 55.77 | 0.2998 | 0.53759 | | |

### *Power attenuation test*

To investigate the effect of the distance in RFID tag performance, as described previously, we employ power attenuation test. The results of the rotation tests are used as an input for power attenuation tests for choosing the fixed angle to experiment with. The strongest angle of rotation in terms of the response rate is chosen for power attenuation tests for the pharmaceutical dosage form in the *XY*-plane (i.e., empty container—270°, purified water—330°, Solution 1—90°, tablet—240°, cream, powder, and coated tablets—210°). Meanwhile, the angle of rotation in *XZ*-plane is fixed at 0° for all dosage forms. For each pharmaceutical dosage form, the attenuation level in RF signal emitted by the interrogator antenna is increased in 3 dB increments until the attenuation level of 15 dB is reached. The curves of the response rate with respect to dosage forms are given in Figure 10.

These curves provide an interesting observation. For nearly all dosage forms, normally we expect to see a monotonically decreasing trend. However, most curves show that the response rates initially increase to a certain point and then begin to decrease after a certain level of attenuation. The trend is in parallel with the

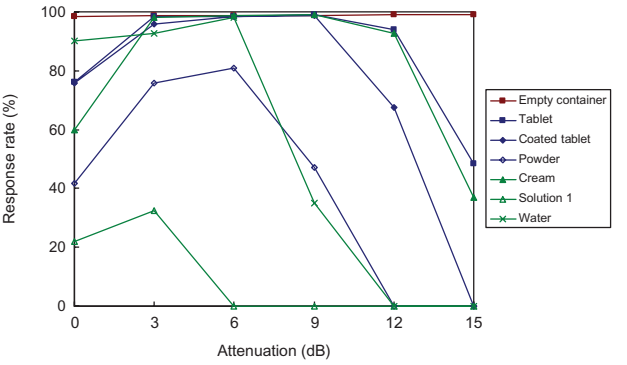


**Figure 10.** Attenuation charts for seven dosage forms.

results reported by Deavours et al.[20] We believe that this reflects the nature of UHF tags. In the antenna design of UHF tags, more consideration is usually given to the performance in far field. Therefore, the tag readability may not be the best when the attenuation is small, or equivalently, the tag is placed very close to antenna. However, we cannot rule out the contribution of other factors such as the environmental noise. Other findings from the curves are consistent with those from rotation tests. Empty container has the best performance, whereas Solution 1 exhibits the worst readability at any attenuation level. Tablet has higher readability than coated tablets beyond an attenuation level of 9 dB, whereas powder constantly has lower readability than tablet or coated tablets. Table 7 lists the threshold interrogator power attenuation levels beyond which the response rate starts to decrease, as well as the power attenuation level, at which the response rate drops to 0%.

### *Ionization impact test*

The ionization test aims to identify the relation between the response rate and the level of ions in the pharmaceutical product. Table salt is soluble in most of the pharmaceutical products in liquid form and releases

**Table 7.** Threshold power attenuation level for different dosage forms.

| Dosage form | Attenuation threshold level for response rate to decline (dB) | Attenuation level for response rate dropping 0% (dB) |
|---|---|---|
| Empty container | >15 | >15 |
| Tablet | 12 | >15 |
| Coated tablet | 12 | 15 |
| Powder | 9 | 12 |
| Cream | 12 | >15 |
| Solution 1 | 6 | 6 |
| Purified water | 9 | 12 |

anions (i.e., $Cl^-$), and cations ($Na^+$) upon dissolving. By intuition, these charged ions might have a negative effect on the response rate. The experiment starts with adding 100 mg of table salt to 67 mL of Listerine™. After adding 100 mg of table salt, the response rate is calculated. This step is repeated in succession until no signal is received by the interrogator (i.e., the response rate drops to 0%). The change of response rate with respect to concentration is shown in Figure 11. There is not an obvious statistical relationship between response rate and concentration, especially before the concentration reaches 4.5 mg/L. It means that before the concentration reaches some certain level, the amount of ions in the solution will have relatively less impact on RF signal transmission. However, beyond the concentration level of 4.5 mg/L, the response rate starts to decline until it reaches zero at the concentration of 13.5 mg/L. The dashed line is the predicted decreasing trend with a rate of −0.095, which means when the concentration increases by 1 mg/L, there is a 9.5% decrease in the response rate.

### *Discussion*

The dosage forms and the angle of rotation significantly affect the response rate of RFID tags in both *XZ*- and *XY*-planes. ANOVA also indicate the interaction between two factors should not be neglected. Each dosage form has a favorable range for rotation angle for RFID tag performance, and these ranges for different dosage forms do not necessarily coincide. The difference in the performance among the pharmaceutical dosage form can be linked with various factors such as the surface waves in the material, the diffraction pattern around the material, and various characteristic material properties (e.g., permittivity and loss tangent)[21]. Usually, compatible dosage forms provide similar results in terms of RFID tag performance suggesting that particle size and base material might play a significant role for the determination of RFID tag readability.

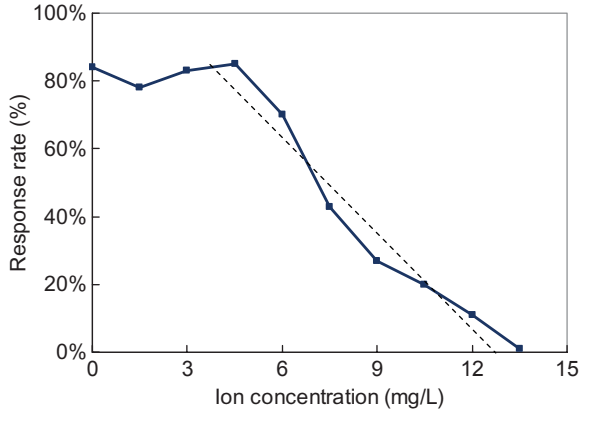


**Figure 11.** Response rate of RFID tag with respect to the ion concentration.

The results of the experiments reveal interesting pieces of information that require further attention. Figure 4A–G indicates that RF read rate for most of the dosage forms do not possess symmetric property with respect to 0–180° axis. Normally, we expect to see such a symmetric pattern because of the RFID tag symmetricity with respect to this axis. However, the fact that tags are placed close to the boundary between the near and the far field of the RFID communication space might cause a shift in the axis of symmetry. In the near field or the region close to near field, the electric and magnetic field components have different angular and radial dependence, and some components that are not significant in the far field are active in this region[22]. These factors that can be neglected in the far field might play an important role in this shift. Another reason might be due to nonhomogenous distribution of cream, coated, and uncoated tablets in the pharmaceutical product container. Nonhomogenity is mainly due to the particle size and material properties of these dosage forms. These products cannot fill the pharmaceutical container homogenously, which in turn leads to perturbation in the overall pharmaceutical container symmetry, thereby causing a shift. The intrinsic properties of material can also induce asymmetry as well. Griffin et al.[21] experiment with RFID tags that are attached to commonly used materials, such as cardboard, pine plywood, ground beef and aluminum slab, and report the performance of RFID tags operating at UHF frequency on these materials. In some cases, they observe that the type of the material might introduce asymmetry and/or lead to some weak or strong points in terms of RFID tag performance with respect to angle of rotation[21]. Another factor that might cause the asymmetry might be the presence of environmental noise. Without the anechoic chamber, it is difficult to eliminate the effect of ambient environment noise because of the existence of objects such as computers, machinery, and human operators. Nevertheless, this effect should not be as significant as the former two because the container is kept close to the RFID antenna and thus the signal reflection or absorption by the objects is controlled to some extent.

As expected, in general the tags attached to empty pharmaceutical containers have a better performance in terms of RFID tag readability as compared with the tags attached to other pharmaceutical dosage forms. This finding is in line with literature that the tags attached to empty containers perform better as compared with others[23,24]. Examining Figures 4A and 5A, it can be seen that the tags attached to these containers have high response rate excluding one instance in *XY*-plane (i.e., 120°). We conclude that the angle of rotation

does not play a significant role on the performance of RFID tags attached to the empty containers. The findings are in concert with the results reported in the literature[24]. Also, it is observed that the RFID tags attached to containers with creams, coated, or uncoated tablets perform better than the tags attached to the containers having Solution 1 and powder. The difference partly stems from the presence of air space in the container induced by the geometry of tablets and coated tablets, and the viscous properties of cream. The air space reduces the interference of RFID signal[24].

In the literature, low read rates for RFID tags attached to water bottles are reported[24,25]. Water degrades the performance of RFID tags especially in UHF range[26,27]. However, contrary to the previous findings, the RFID tags attached to containers with purified water perform moderately well. It might be attributed to the fact that the RFID tag is placed close to the boundary between near and far field of the interrogator antenna in our experiments. In the near field of the interrogator antenna, the field intensity is much more higher compared with the far field and less energy is required for activating the tag, which means that these tags can function in nonfriendly RF environment[22]. Besides, the separation of the RFID tag and the purified water because of the wall thickness of the pharmaceutical container might also contribute to the response rate. This can be further supported by the result of Ramakrishnan, who indicates that RFID tag readability improves when the distance between the RFID tag and liquid is increased[19].

The RFID tags attached to Solution 1 perform very poorly. The active ingredient of Solution 1 is glycerin. A chemical that is similar to glycerin in terms of molecular structure (i.e., ethylene glycol) is reported to have relatively higher average gain penalty compared with other materials. In general, RFID tags perform poorly in the proximity of materials with high average gain penalties[21]. Therefore, it is believed that poor readability of the tags attached to Solution 1 might be also related with the probable high average gain penalties associated with the glycerin.

The response rate increases slightly when the attenuation of signal-transmitting power decreases for all pharmaceutical dosage forms. After a certain threshold level, the readability of RFID tag deteriorates. Generally, the power of electromagnetic signal decreases in proportion with the square of distance between the interrogator antenna and the RFID tag[28]. This effect leads to deterioration of RFID tag readability with increased distance. However, slight increases in the read rate with the increasing signal attenuation levels are reported for the tags that are placed on the boundary between near and far field of the interrogator antenna[29]. These findings are in line with the results obtained in our study.

Similar to the case of the signal-transmitting power, there is a threshold value for the ion concentration in Listerine™ solution. Initially, the response rate of the RFID tag fluctuates within a relatively smaller band (i.e., $\approx 82.5 \pm 2.5\%$) with an increase in concentration. Beyond a certain threshold value, the response rate deteriorates. When the dipole-type antenna is brought close to some metal, it will form negative image currents into the material according to the image theory. This reduces the radiation efficiency of the dipole-type antenna[30]. The Impinj Satellite Generation 2 RFID tag employed in our experiments has a hybrid design featuring loop/dipole configuration. We hypothesize that the anions introduced by adding salt in the Listerine™ solution acts like free electrons in metallic objects and negative currents are induced by RFID signal. Higher ion concentration leads to stronger negative currents and further deterioration in RFID tag performance.

As previously stated, to the best of authors' knowledge, there is no published research work that provides a comprehensive analysis of the factors on readability of RFID tag attached to pharmaceutical products so far. In addition to that, there are a very limited number of publications that address RFID tag performance in the literature. Moreover, there is no standard procedure for evaluating and benchmarking RFID tag performance to date. For this reason, the comparison of our findings with previous work is extremely difficult; however, the discussion, based on the knowledge in related fields, provides insightful information for the results obtained in the experiment.

## Conclusions

Item-level tagging of pharmaceutical products using RFID technology will significantly improve the security and efficiency of pharmaceutical distribution. It can also become a viable method for ensuring absolute authenticity of the medicines, which is critical for patient safety[3]. Investigation of how an RFID system performs with different dosage forms of pharmaceutical products at item level is an important step toward this goal. The results of this study cannot only provide guidance for the drug manufacturers to implement this technology but also help the RFID technology providers to develop more suitable products for pharmaceutical applications. The factors that are reckoned to be important for RFID system performance are tested using the experimentation scheme outlined in the previous sections and their significances are evaluated utilizing various statistical procedures. The general finding of the study is that all the factors that are analyzed in this research play significant role on RFID tag readability, and system performance can be considerably improved by selecting the optimum levels of these factors. However, there is no generic

solution that is applicable for all the cases and, depending on the pharmaceutical dosage forms, the adjustment might be required to improve system performance.

As previously indicated, we present a pilot and yet fairly comprehensive study on the RFID performance with pharmaceutical products, but the research should be extended in the future. For future research, other dosage forms such as gels and suspensions will be included. Gels are semisolid systems made of suspensions, and suspensions are finely divided solids that are dispersed in a solid or liquid. Understanding the performance of solid and liquid dosage forms may shed light on predicting the effect of gels and suspensions used as dosage forms on RFID tag readability. However, direct experimentation with gels and suspensions is necessary. Also, in order to better understand the effect of the dosage form on response rate, future research might consider increasing the variety of products within the same dosage form. For example, in addition to Aspirin, Advil™ tablets might also be included in the analysis for a better understanding of the effect of tablets on RFID tag response rate.

***Declaration of interest:*** The authors report no conflicts of interest.

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