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# Development of Diabecine™ Tablet and Confirmation of Its Physical Properties and Pharmaceutical Safety Analysis

(Pembangunan Tablet Diabecine™ dan Pengesahan Sifat Fizikal dan Analisis Keselamatan Farmaseutikal)

TEH LIAM CHEE*, FADZILAH ADIBAH ABDUL MAJID & MOHD CAIRUL IQBAL

ABSTRACT

*Herbal medicine is usually made using dry powdered herbs in the form of capsule. Capsule form herbal supplement suffers lower shelf life as compared to compact herbal powder in tablet form. In this study, Diabecine™ , a blend of herbal medicine traditionally used as herbal supplement for diabetic patients was selected and transformed into a compressed tablet. Direct compression method and minimal usage of excipients were the aims of this study. By using direct compression, the blend of 40% fine powder herbs and 60% of excipients performed the best and fulfill the pharmaceutical standard. The safety data of microbial and heavy metal testing obtained met the safety requirements for herbal supplement category under the National Pharmaceutical Control Bureau of Malaysia. In conclusion, the tablet formulation of Diabecine™ is suitable to be manufactured by using direct compression method. This research implicates the possibility of producing tablets with high dose of herbal powder by direct compression method.*

*Keywords: Direct compression; FTIR; herbal supplement; impurity; tablet characteristic*

ABSTRAK

*Ubat herba biasanya diperbuat daripada serbuk kering herba dalam bentuk kapsul. Suplemen herba dalam bentuk kapsul mempunyai jangka hayat yang lebih rendah berbanding dengan serbuk herba yang dipadat dalam bentuk tablet. Dalam kajian ini, Diabecine™ , satu campuran ubat herba yang digunakan secara tradisi sebagai suplemen herba untuk pesakit kencing manis telah dipilih dan diubah menjadi mampatan tablet. Kaedah pemampatan terus dan penggunaan eksipien yang minimum adalah matlamat kajian ini. Dengan menggunakan pemampatan terus, campuran mencapai prestasi yang terbaik dan memenuhi piawaian farmaseutikal. Data keselamatan ujian mikrob dan logam berat yang diperoleh telah memenuhi keperluan keselamatan bagi kategori suplemen herba di bawah Biro Pengawalan Farmaseutikal Kebangsaan Malaysia. Kesimpulannya, formulasi tablet Diabecine™ adalah sesuai untuk dimampatkan dengan menggunakan kaedah pemampatan terus. Kajian ini mengimplikasikan kemungkinan untuk menghasilkan tablet dengan dos serbuk herba yang tinggi dengan kaedah pemampatan terus.*

*Kata kunci: Cemaran; ciri tablet; FTIR; pemampatan terus; suplemen herba*

## INTRODUCTION

Herbal plants based traditional medicine systems had been existed for thousands years (Cragg & Newman 2005). Although the traditional herbal medicines widely trusted due to their efficacy but the products are often being criticized due to lack of standardization and poor presentation (Gbenga & Olabanji 2013; Majekodunmi & Odeku 2009). Up till now, the design and formulation of herbal tablet is still very challenging task due to poor tableting properties of the herbs and their dried extract (Chaves et al. 2009; Ghiware Nitin B. 2010). There are still very few researchers applying the technique of design of experiments (DOE) in developing direct compressed herbal tablet and most of these researches are done in India (Ganapaty et al. 2013; Ramaiah et al. 2013; Savarikar et al. 2011).

In this research, Diabecine™ was selected as the traditional antidiabetic formulation to be transformed from raw powder in hand filling capsule form into herbal tablets via direct compression. This particular formulation has been prescribed by an Indonesian traditional practitioner to diabetic patients in the form of hand filling capsules for more than 50 years. Until this study, Diabecine™ is a homemade product from a few types of herbs with no scientific evidence and R&D to improve its appearance and standardize its dosage. The produced tablets were studied for their tablet characteristics (weight, hardness, friability and disintegration time) and drug-excipient compatibility to ensure they comply with the pharmacopoeia standard. The tablets were also been tested on their safeness via heavy metals and microbiological analysis based on the requirements of NPCB, Malaysia.

## MATERIALS AND METHODS

The herbal formulation that was developing into antidiabetic tablet in this research was supplied by a traditional herbal medicine producer Millenium Multiherbs,

Johor. It contains several medicinal plants powders such as Indonesian bay leaves (*Syzygium polyantum*), king of bitters (*Andrographis paniculata*), Java tea (*Orthosiphon stamenius*), Ceylon cinnamon (*Cinnamon verum*) and Javanese tumeric (*Curcuma xanthorrhizae*). The herbs were grinded and passed through a 200 μm sieve, those powders retained in the sieve were collected, regrind and sieve again. The powders were than mixed well and keep at cold, dried place for further use.

### DESIGNING OF DIRECT COMPRESSED TABLET

The designs of experiments were done by Design-Expert® software. Formulations were developed following the D-optimal mixture design which is a design that is flexible enough to accommodate design constraints and model changes. The coordinate of 17 design points for the constrained were generated and randomly arranged by Design-Expert®. Three constituents were mixed according to the design with multiple constraints on the component proportions as stated in Tables 1 and 2. The mixtures of powders were then kept in air-tight container and labeled. Direct compressions of tablets were carried out by rotary tableting machines located in Institute of Bioproduct Development, Universiti Teknologi Malaysia.

### TABLET CHARACTERISTIC

The characteristic of tablets were determined by test apparatuses located at Faculty of Pharmacy, Universiti Kebangsaan Malaysia.

### WEIGHT MEASUREMENTS

The weights of tablets were measured using tablet weighting tool (Sartorius) by weighting 20 tablets individually and calculate the average of weight for the samples. Comparison was then made between the individual tablet weights and the average weight. The amount of tablets differs from the average weight must be less than two tablets and should not exceed the percentage as listed in Table 3. No tablet must differ by more than double the relevant percentage.

### HARDNESS, DIAMETER AND THICKNESS MEASUREMENTS

Tablet crushing strength (hardness), tablets diameter and thickness was checked by carried out hardness measurement by using 3 in 1 hardness tester (Model PTB311E, Pharma-test) where a random samples of (ten tablets) was taken and allow to age for 24 h after production. The samples were tested individually using automate 3 in 1 tablet testing instrument and each value reported is a calculated average of ten measurements. Normally oral tablets should have hardness from 4-10 kg while some sustained release tablets are 10-20 kg which is much harder.

### FRIABILITY

The friability of tablets was measured by Roche Friabilator (Copley) where 20 tablets were chosen randomly and weighed. The tablets were then placed in the friabilator and exposed to rolling and continual shocks as they fall 6 inches in each turn within the friabilator. After 100 revolutions, the final weights of tablets were taken. Comparison was made between the reading of initial and final weight. Tablet friability is the loss due to abrasion and it will be expressed as a percentage. Any cracked tablets were excluded from the calculation and the maximum acceptable weight loss is less than 1% of the weight of tablets being test (Odeku 2008).

### DISINTEGRATION TIME

Disintegration times of developed tablets were determined by using tablet disintegration test apparatus (Copley Scientific). For uncoated tablet, the disintegration time was tested by placing one tablet in each of the tubes of the basket and adds a disk to each tube on top of the tablet. Operate the apparatus, using water or the specified medium as the immersion fluid, maintained at 37 ± 2°C. At the end of 15 min, lift the basket from the fluid and observe the tablets: All of the tablets disintegrate completely. If 1 or 2 tablets fail to disintegrate completely, repeat the test on 12 additional tablets. The requirement is met if not less than 16 of the total of 18 tablets tested disintegrate completely (Davydova 2008).

### HEAVY METALS AND MICROBIOLOGICAL ANALYSIS OF DEVELOPED TABLETS

After the analysis of tablet characteristic, the tablet formulation with best performance was selected and subjected for element testing to test the availability of inorganic element content such as cadmium, mercury, arsenic and lead. It was also subjected for microbiological testing to assess the safety of raw materials. The microbiological testing include testing the existence of

TABLE 1. Variables and intervals selected to perform the mixture design

| Variables | Level | |
|---|---|---|
| | Low | High |
| A=fraction of Diabecine™ | 30 | 55 |
| B=fraction of MCC | 45 | 70 |
| C=Fraction of Aerosil | 0 | 1 |

*The amount of total mixture, A+B+C=100%*

TABLE 2. DOE parameter proportion (%) in the mixture

| Run | A:Diabecine™ | B:MCC | C:Aerosil |
|---|---|---|---|
| 1 | 53.572 | 45.428 | 1.000 |
| 2 | 50.274 | 49.123 | 0.603 |
| 3 | 33.014 | 66.986 | 0.000 |
| 4 | 53.572 | 45.428 | 1.000 |
| 5 | 40.346 | 59.105 | 0.549 |
| 6 | 43.440 | 55.565 | 0.995 |
| 7 | 37.938 | 62.062 | 0.000 |
| 8 | 47.099 | 52.901 | 0.000 |
| 9 | 30.000 | 70.000 | 0.000 |
| 10 | 54.705 | 45.000 | 0.295 |
| 11 | 47.099 | 52.901 | 0.000 |
| 12 | 35.061 | 63.939 | 1.000 |
| 13 | 54.705 | 45.000 | 0.295 |
| 14 | 30.000 | 70.000 | 0.000 |
| 15 | 30.000 | 69.003 | 0.997 |
| 16 | 30.000 | 69.003 | 0.997 |
| 17 | 42.252 | 57.252 | 0.497 |

*Each run composition was random and arranged according to mixture design D-optimal model provided by the Design Expert ® software*

TABLE 3. Weight variation requirement

| Average weight | Percent difference |
|---|---|
| 130 mg or less | 10 |
| More than 130 mg through 324 mg | 7.5 |
| More than 324 mg | 5 |

*Escherichia coli, Salmonella, Staphylococcus aureus, Enterobacteriaceae* and certain other gram negative bacteria, total plate count and total yeast and mould count. These independent tests were conducted by Chemical Laboratory (Malaysia) Sdn. Bhd. by referring to the British Pharmacopoiea (2004). The samples are required to pass these tests in order to fulfill the requirement of NPCB, Malaysia as a registrable traditional medicine.

### HERBS-EXCIPIENT COMPATIBILITY STUDY

The Diabecine™ polyherb powder, powdered F5 tablet, Aerosil, microcrystalline cellulose and the mixture of excipients (Aerosil with MCC) were subjected to IR spectroscopic study using FT-IR spectrophotometer (Spectrum One, Perkin-Elmer) in Universiti Teknologi Malaysia by employing standard KBr pellet technique. The sample powder was grind with potassium bromide (KBr) in the ration of 1:100 (2 mg of sample in 200 mg of KBr). The mixture was then being placed in the mold and pressed to form the thin pellet (approximately 1 mm in thickness and 5 mm in diameter. The mold and pellet was then placed in the FTIR machine and read for the spectra. The spectra were scanned over the wave number range from 4000 - 370 $cm^{-1}$ in order to determine the herbs-excipients compatibility. FTIR spectrums were read as percent transmission (% T).

## RESULTS AND DISCUSSION

### ASSESSMENT OF THE MECHANICAL STRENGTH OF TABLETS

According to U.S. Pharmacopeia, the mechanical strength of tablets is of considerable importance and is routinely measured as a guideline for product development and as a quality control requirement. Tablets cannot be too hard in view of the fact that it may affect the disintegration or drug release profile (Kim 2009). While the measurement of the tablets' breaking force (commonly called hardness) provides some indication of the tablets' mechanical robustness, it does not accurately measure the ability of the tablets to withstand the handling they will come across during processing and shipping. Therefore, a friability test is designed to determine the weakness of tablets and assess the resistance of the tablet surface regions to abrasions or other forms of general damages (<1217>2009), (Banker et al. 2002). These two tests are usually employed to measure the mechanical strength of a tablet.

Table 4 shows the hardness, thickness and diameter of tablets for each formulation. Values are expressed in mean ± SD, $n$=20. The thicknesses of the tablets ranged from 4.94 ± 0.06 to 5.26 ± 0.02 mm and diameter from 9.56 ± 0.03 to 9.64 ± 0.02 mm. The tablet hardness of different formulations ranged from 25.3 ± 1.1 N to 148.9 ± 14.9 N. A normal tablet should have a hardness value ranged from 40 to 100 N. Thus, the tablets of F2, F4, F10, F13, F15 and F16 were failed in the hardness test because their hardness value is out of the acceptable range.

The tablet friability was determined according to procedure provided in U.S. Pharmacopeia using a friability tester. One percent of weight loss is considered as the maximum acceptable mean weight loss for the samples.

Table 4 indicates that all samples pass the friability test with less than 1% weight loss. Weight loss of all 17 formulations ranged from 0.087 to 0.823%. The sample with greatest weight loss was sample F13, with 0.823% of weight loss. Although it meets the friability standard of less than 1% weight loss, this formulation has the least crushing strength (25.3 ± 1.1 N) and it is most friable and hence is not ideal as tablets.

Crushing strength-friability ratio (CSFR) is an index of measuring tablet quality by comparing the measurement of tablet strength (hardness) and weakness (friability). It was calculated by dividing the crushing strength by the friability. The effect of formulation changes on the tablet mechanical strength can be evaluated by referring to the CSFR value of the tablets. Generally, the higher the CSFR value, the stronger the tablet is (Adetunji et al. 2006; Gbenga & Olabanji 2013; Majekodunmi & Odeku 2009). The CSFR for the 17 formulations ranged from 31.46 to 1556.114. Basically, when the proportion of MCC increased, the hardness of the tablets increased and as a result, CSFR also increased. As shown in Table 4, of all the formulations, F16 showed the highest CSFR while F13 had the lowest. By referring to the measured hardness, friability and CSFR, we can conclude that tablets made from F13 were the weakest among all because it has the lowest CSFR ratio, highest weight loss in friability test and lowest hardness value.

The disintegration test was carried out to determine the time required for a tablet to completely disintegrate when immersed in a certain test fluid. The maximum allowed disintegration time for an uncoated tablet is 15 min (2006). The disintegration of a tablet in the gastrointestinal tract is a crucial step in absorption and bioavailability through the epithelial membranes (Ibezim et al. 2008). Generally, fast disintegrating tablets do not necessarily guarantee fast bioavailability but slow disintegrating tablets almost assure slow bioavailability for all the time (Carter 2006). The tablet must disintegrate into its primary particles as quickly as possible to achieve optimal dissolution of active constituent and result in higher bioavailability (Gibson 2001). In this experiment, all tablets disintegrated completely within the standard time limit of 15 min and passed the disintegration test. The short periods of disintegration time are possibly due to the presence of large amounts of disintegrant (microcrystalline cellulose). The average weight of tablets for the difference formulations ranged from 0.332 ± 0.003 to 0.377 ± 0.009 g. The average content of Diabecine™ polyherb was calculated by multiplying the mean weight of produced tablet with the percentage of Diabecine™ powder (AI) in the same formulation. Thus the average content of AI in one tablet for the different formulations ranged from 111 ± 0.002 to 190 ± 0.004 g. From Table 5, it shows that all samples passed the weight variation test except sample F7 and F12. Both sample F7 and F12 have more than 50% of MCC. MCC is an excipient that functions as a glidant, disintegrant and binder with good flow properties, therefore there is a high possibility they failed the test due to human error or errors occurred during the mixing or tableting process for these particular formulations.

Among the formulations that passed all the physical quality examinations as discussed previously, tablet of F5 and F14 possess the highest CSFR values, which is 1065.46 and 635.61, respectively. Although tablets of F14 have a lower weight lost percent in friability test and higher hardness value if compared to tablets of F5, but F14 contained less amount of Diabecine™ (30%)

TABLE 4. Hardness, thickness, diameter, friability and CSFR of tablets

| Batch | Hardness, N (Mean±SD), *n*=20 | Thickness, mm (Mean±SD), *n*=20 | Diameter, mm (Mean±SD), *n*=20 | Friability, % | CSFR | Disintegration time (s) |
|---|---|---|---|---|---|---|
| F1 | 54.6 ± 6.7 | 5.19 ± 0.05 | 9.61 ± 0.01 | 0.184 | 296.96 | 40 |
| F2 | 37.7 ± 1.9 | 5.26 ± 0.02 | 9.63 ± 0.03 | 0.322 | 117.00 | 22 |
| F3 | 54.2 ± 2.9 | 5.13 ± 0.02 | 9.59 ± 0.01 | 0.211 | 256.44 | 38 |
| F4 | 39.4 ± 4.2 | 5.19 ± 0.03 | 9.62 ± 0.02 | 0.241 | 163.12 | 26 |
| F5 | 86.3 ± 8.1 | 5.19 ± 0.04 | 9.58 ± 0.01 | 0.136 | 635.61 | 56 |
| F6 | 55.9 ± 3.5 | 5.20 ± 0.02 | 9.61 ± 0.01 | 0.313 | 178.76 | 31 |
| F7 | 76.8 ± 12.0 | 4.94 ± 0.06 | 9.57 ± 0.01 | 0.240 | 320.15 | 42 |
| F8 | 42.3 ± 1.6 | 5.04 ± 0.03 | 9.58 ± 0.01 | 0.282 | 150.27 | 29 |
| F9 | 88.5 ± 10.9 | 5.18 ± 0.04 | 9.57 ± 0.01 | 0.188 | 470.97 | 46 |
| F10 | 33.3 ± 3.3 | 5.05 ± 0.02 | 9.61 ± 0.01 | 0.335 | 99.40 | 17 |
| F11 | 43.0 ± 2.9 | 5.12 ± 0.03 | 9.62 ± 0.01 | 0.409 | 105.07 | 24 |
| F12 | 110.8 ± 4.7 | 5.24 ± 0.03 | 9.57 ± 0.02 | 0.127 | 870.68 | 60 |
| F13 | 25.3 ± 1.1 | 5.21 ± 0.01 | 9.64 ± 0.02 | 0.823 | 31.46 | 10 |
| F14 | 92.6 ± 9.2 | 5.12 ± 0.05 | 9.56 ± 0.03 | 0.087 | 1065.46 | 88 |
| F15 | 134.2 ± 13.6 | 5.16 ± 0.06 | 9.57 ± 0.02 | 0.122 | 1098.77 | 85 |
| F16 | 148.9 ± 14.9 | 5.17 ± 0.07 | 9.57 ± 0.02 | 0.096 | 1556.11 | 90 |
| F17 | 52.5 ± 3.6 | 5.20 ± 0.03 | 9.62 ± 0.03 | 0.261 | 201.55 | 35 |

TABLE 5. Weight variation of tablets

| Formulation | Weight, g (Mean ±SD), *n*=20 | Average amount of API per tablet, mg (Mean ±SD), *n*=20 | Verdict |
|---|---|---|---|
| F1 | 0.355 ± 0.008 | 190 ± 0.004 | passed |
| F2 | 0.352 ± 0.003 | 177 ± 0.001 | passed |
| F3 | 0.348 ± 0.004 | 115 ± 0.001 | passed |
| F4 | 0.340 ± 0.004 | 182 ± 0.002 | passed |
| F5 | 0.375 ± 0.009 | 151 ± 0.003 | passed |
| F6 | 0.352 ± 0.004 | 153 ± 0.002 | passed |
| F7 | 0.346 ± 0.012 | 131 ± 0.005 | failed |
| F8 | 0.341 ± 0.004 | 160 ± 0.002 | passed |
| F9 | 0.373 ± 0.007 | 112 ± 0.002 | passed |
| F10 | 0.332 ± 0.003 | 182 ± 0.002 | passed |
| F11 | 0.341 ± 0.008 | 161 ± 0.004 | passed |
| F12 | 0.368 ± 0.022 | 129 ± 0.008 | failed |
| F13 | 0.335 ± 0.004 | 183 ± 0.002 | passed |
| F14 | 0.371 ± 0.006 | 111 ± 0.002 | passed |
| F15 | 0.377 ± 0.009 | 113 ± 0.003 | passed |
| F16 | 0.377 ± 0.008 | 113 ± 0.002 | passed |
| F17 | 0.353 ± 0.004 | 149 ± 0.002 | passed |

in the formulation. Thus, tablets of F5, with 40.35% of Diabecine™ in the formulation, were selected as the best performed tablets. Quality control tests and safety monitoring of herbal products are crucial to ensure the patients can ingest herbal medicines safely. Unregulated products and ineffective quality control may lead to serious public health concerns. F5 tablets were later subjected to further safety evaluation based on the requirements of NPCB, Malaysia.

### SAFETY ASSESSMENT OF SELECTED (F5) TABLET HEAVY METAL ANALYSIS

Herbal products are created from natural resources such as plants and therefore may contain heavy metals absorbed from fertilizers, pesticides and polluted water or soil during growth (Yuan et al. 2009). Heavy metals such as mercury, arsenic, cadmium and lead are toxic to humans. For this reason, it is essential to determine the quality of herbal products by carrying out a heavy metal analysis.

The Independent heavy metal limit tests on F5 tablet were carried out by Chemical Laboratory (Malaysia) Sdn. Bhd. As shown in Table 6, all tested metallic elements were not detected in the samples. The acceptance criteria of heavy metal limit test were set by referring to Drug Registration Guidance document by National Pharmaceutical Control Bureau, Malaysia (2013). Therefore, in respect to heavy metals, F5 tablets are safe for consumption. The results of heavy metal limit test were shown in Table 6. There was no detection of lead, arsenic, mercury and cadmium in the samples.

### MICROBIOLOGICAL ANALYSIS ON F5 TABLETS

Herbal plants may be contaminated with 'invisible' bacteria, fungi and viruses due to naturally occurrence or poor handling and can cause toxicity to the final products (Bandaranayake 2006). Independent microbial analyses were carried out to investigate the existence of microbial contamination. The results in Table 7 shows that all the tested results were within acceptable criteria according to the British Pharmacopeia 2013, Appendix XVI and Drug Registration Guidance Document by National Pharmaceutical Control Bureau of Malaysia. There were insignificant amounts of aerobic microbes detected in the total plate count while the other tested microbes were absent in F5 tablets.

Herbs-excipients Compatibility Study and Functional Groups Identification Drug-excipient compatibility plays a key role in the release of drug thus it is necessary to check the drug compatibility with the excipient while developing a new formulation. While most of the excipients are

TABLE 6. The content of heavy metals in a F5 tablets

| Parameters | Methods | Acceptance criteria | Results |
|---|---|---|---|
| Lead, Pb | Acid Digestion/ AAS | NMT 10.0 ppm | Not detected |
| Arsenic, As | Hydride Generation / AAS | NMT 5.0 ppm | Not detected |
| Mercury, Hg | Hydride Generation / AAS | NMT 0.5 ppm | Not detected |
| Cadmium, Cd | Acid Digestion/ AAS | NMT 0.3 ppm | Not detected |

NMT: Not More Than

TABLE 7. Microbiological quality of F5 tablet

| Parameters test | Methods | Acceptance Criteria | Results |
|---|---|---|---|
| Total plate count, cfu/g | BP 2004 | NMT $2\times10^5$ CFU | $7.2 \times 10^2$ |
| *E. Coli* in 1 g | BP 2004 | NMT $2\times10^2$ CFU | Absent |
| *Salmonella* in 10 g | BP 2004 | NMT $2\times10^3$ CFU | Absent |
| *Staphylococcus aureus* in 1 g | BP 2004 | Absence | Absent |
| *Enterobacteriaceae* and certain other gram negative bacteria | BP 2004 | Absence | Absent |

NMT: Not More Than; BP: British Pharmacopeia
Total Plate Count: Total Aerobic Microbial Count

considered inert, there are some specific excipients that are incompatible with certain materials (Rowe et al. 2009). Excipient-drug interaction and poor quality excipients may contribute to the instability of the active substance or other quality issues.

In recent years, FTIR (Fourier Transform Infrared) spectroscopy has made a remarkable role in the field of medicinal plant analysis. It is used as a rapid quality control for herbs and is able to detect any changes in the physical and chemical constitution of drug-excipient mixtures. In this case, the pure drug and physical mixture of drug and excipient were subjected to FTIR detection. The IR spectra of the drug before and after combining with excipient were compared and observed changes in the main peaks. If there were no changes in the main peaks for the spectra of drug and drug-excipient, it means there was no interaction between the drug and excipient (Chen et al. 2010; Deepak et al. 2011; Gilhotra et al. 2013; Jain et al. 2010).

Usually, commercial IR spectrometer covers 4000-400 $cm^{-1}$ (Nair et al. 2013). A frequency region of 4000-1300 $cm^{-1}$ is the region for functional groups while 1300 $cm^{-1}$ and below are the fingerprint region (Ning 2011). Absorption occurs when the IR radiant energy matched to the energy of specific molecular vibration. As a result, the spectrum of each sample is unique, as no different molecular structure can produce the same spectra (Joshi 2012).

In this study, the F5 excipient mixture (which contain 0.55% of Aerosil and 59.10% of MCC according to the formulation in F5 tablet), Diabecine™ raw polyherb and F5 tablets were both examined via FTIR to identify the drug-excipient compatibility and the existence of functional groups in the formulation. From the spectra recorded, the main peaks' values in both Diabecine™ and F5 tablet (Figure 1) were found to be very similar. This means that there are no chemical interactions or physical changes between the active ingredient and excipients used.

This study has proven that direct compression of tablets containing high dosages of polyherbal powder is achievable. On top of that, Diabecine™ tablets have passed all of the pharmaceutical tests conducted and therefore have proven their good physical properties and safety. However, due to limitations of resources and time, bioavailability tests of the Diabecine™ tablets were not carried out. Also, although Diabecine™ tablets have passed the disintegration test, their disintegration time is quite short. Therefore, the authors suggested coating these tablets in order to prolong the disintegration time and improve the appearances of these tablets.

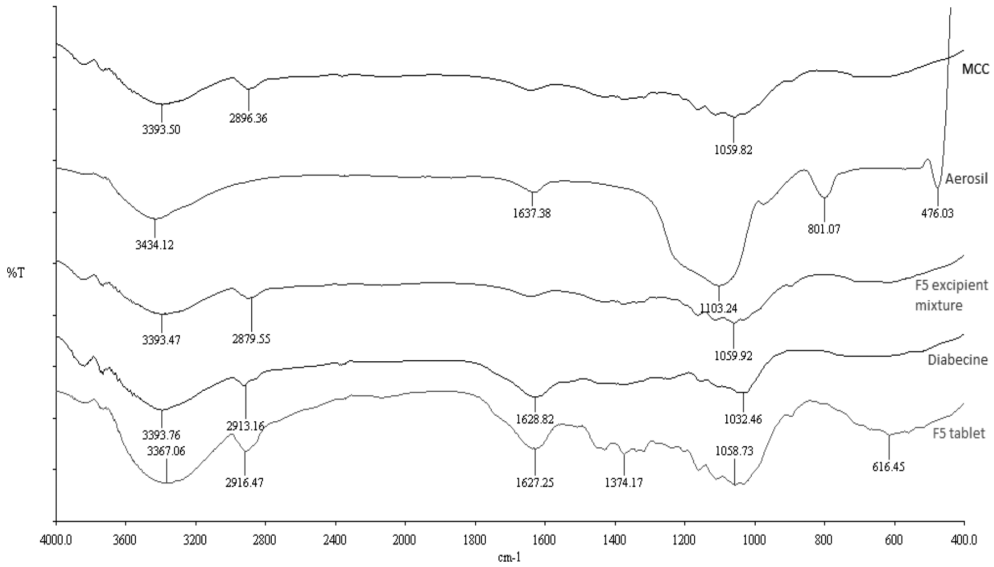


FIGURE 1. FTIR Spectrum for MCC, Aerosil, F5 excipient mixture, raw Diabecine™ polyherb powder and F5 tablet

## CONCLUSION

This study was intended to convert a traditional polyherbal formulation, Diabecine™ , from hand-filing capsules into modern oral tablets via direct compression that complied with pharmacopoeia standards and the NPCB, Malaysia requirements. It was found that tablets with the formulation of 40.35% Diabecine™ polyherb powder, 59.10% MCC and 0.55% Aerosil performed best in all physical quality tests. These tablets were found to be free from heavy metals and complied with the microbiological criteria. The herbs were found to be compatible with the excipient. In conclusion, from all the physical evaluation data and safety evaluations, it was found that the tablet formulation of Diabecine™ showed satisfactory results and it is suitable to be manufactured by using direct compression method.

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Teh Liam Chee*
Department of Bioprocess Engineering
Faculty of Chemical Engineering
Universiti Teknologi Malaysia
81310 UTM Johor Bahru, Johor Darul Takzim
Malaysia

Fadzilah Adibah Abdul Majid[2]
Institute of Bioproduct Development (IBD)
Universiti Teknologi Malaysia
81310 UTM Johor Bahru, Johor Darul Takzim
Malaysia

Mohd Cairul Iqbal
Faculty of Pharmacy, Universiti Kebangsaan Malaysia
Jalan Raja Muda Abdul Aziz
50300 Kuala Lumpur, Federal Territory
Malaysia

*Corresponding author; email: lcteh86@gmail.com

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