RELATIVE COMPARISON OF STABILITY AND DEGRADATION OF METHYLCOBALAMIN TABLETS OF DIFFERENT BRANDS AT DIFFERENT STORAGE SETTINGS

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ABSTRACT

Objective: To assess relative comparison of stability and degradation of Methylcobalamin tablets of different brands at various storage circumstances.

Methods: The comparative in vitro study of Methycobal (innovator brand) with its other 5 different brands Cobalamin, Neuromet, Incobal, Qbal and Mecobal was organized for evaluation of physicochemical features of hardness, thickness, friability, weight variation, disintegration time and accelerated stability at 3 temperatures, 25 °C, 30 °C±65 % and 40 °C±75 % respectively for 3 mo. Later all brands were passed through HPLC for checking the extent of degradation of drug products.

Results: All tablet brands were within the weight variation specified limits except Mecobal with a relative standard deviation of 6.83%. The weight variation values of Methycobal, Cobalamin, Neuromet, Incobal, Qbal and Mecobal were 0.29%, 0.11%, 0.09%, 0.13%, 0.09% and 0.14% after friability test respectively as per standard limits. The average thickness of Cobalamin, Incobal and Mecobal were not within specified limits. The average hardness of all trades was within limits except Cobalamin and Mecobal exceeding 6kp. The disintegration time of all companies was as per specifications.

Conclusion: Qbal was found economical and cost-effective. However, study facts unveiled no noteworthy variety in the Q. C assessments of Methylcobalamin brands.

Keywords: Stability, Degradation, Methylcobalamin, Storage

INTRODUCTION

Methylcobalamin, Mecobalamin, McChl, and MeB12 all are declared terms used to identify vitamin B12 [1]. McChl is a therapeutically active segment of vitamin B12, also applied in the management of Alzheimer’s sickness, rheumatoid arthritis [2]. Vitamin B12 is critical for actions of neurons, erythrocytes (RBCs) manufacturing, and is a cofactor for three foremost reactions; the transfer of methylmalonic acid to succinyl coenzyme A; the changing of homocysteine to methionine and the change of 5-methyltetrahydrofolate to tetrahydro folate [5, 6]. Maternal vitamin B12 shortage while pregnancy or during lactation can progress to neural tube faults, malfunction to flourish, hypotonic state, abnormalities in movement, and anemic situation. Females at higher hazard or with recognized deficit need to be supplemented with vitamin B12 throughout pregnancy or during breastfeeding or giving nourishment [7, 8].

There are various preparations applied to lessen the risk of scarcity of vitamin B12 like mucoadhesive buccal tablets, microencapsulated formulations, lozenges, liposomes, buccal films, nose sprays, intranasal drops, transdermal solubilized emulsions, mouth spray, gelatin parenteral dose shape, inhaler/pen, buccal mucosol of hydrogelic films and toothpastes etc [9, 10].

MATERIALS AND METHODS

Study design

Comparative in vitro quality control parameters amongst the commercially available tablet brands of Methylcobalamin innovator brand compared with it’s five other different brands produced in Pakistan.

Chemicals

Methylcobalamin tablets of innovator brand Innov-B and other five Brands Cobalamin, Neuromet, Incobal, Qbal and Mecobal were chosen for the study project. 200 Tablets of each brand were purchased from local medicine market Quetta, Pakistan. Methylcobalamin was gifted by Martin Dow marker. All brands of Methylcobalamin contain 500 mcg.

Reagents for HPLC sampling

Acetonitrile for Chromatographic process (Lichrosolv), Buffer solution pH 3.0+/0.02 (20 °C), [Citrated Hcl], Mecobalamin reference sample, Lichrospher 100 RP-8 end-capped (10 micrometers), Disposable filter 0.45 um.

Instruments

Digital Electronic Balance, Vernier caliper, Disintegrator (Pharma tester), Hardness tester (Pharma tester), Roche Friabilator (Pharma
test), Stability chamber (Binder II-KBF720), HPLC apparatus (Shimadzu, LiChroCART 250-4 HPLC Cartridge) of analytical grade.

Methodology
The relative examination of Methylcobal with other five diverse companies including Cobalamin, Neumert, Incobal, Qbal and Mecobal was systematized for valuation of physical and chemical attributes such as hardness, Thickness and Diameter, Friability, weight variation and accelerated steadiness at 3 temperatures, lab temperature, 30 °C and 40 °C by keeping relative humidity±65% and 75% correspondingly for 3 mo prior to stability testing as well as subsequently. Then innovator brand along with 5 other trades were passed through HPLC test for knowing the degradation of tablets of brands.

Physical evaluation of methylcobalamin tablet brands

Weight variation test
200 tablets of each brand were weighed in isolation with the above-mentioned Digital analytical weighing balance and average weight and the percentage of variance was unveiled for every brand [12]. The equation for calculation of percentage weight variation is given below;

\[
\text{Percentage weight variation} = \left(\frac{\text{average weight}-\text{individual weight}}{\text{individual weight}}\right)\times 100\%.
\]

Thickness test
20 tablets of each brand were employed for thickness determination by Vernier caliper in mm.

Hardness test
Tablet hardness is typically expressed as the load necessary to crush a tablet positioned on its perimeter and hardness is occasionally called tablet crushing force. The appropriateness of the tablet believed to mechanical stability at some point in wrapping and consignment would typically be forecasted on the criteria of hardness. The crushing potency was determined with a tablet hardness tester (Monsanto). Ten tablets were arbitrarily elected from each brand for this test [13].

Friability test
The trial was initiated by weighing 10 tablets overall that is weighed in isolation that apparatus was revolved at 100 rpm for 4 min (25 rpm for 1 min). Then tablets were deducted, and re-weighed (just the intact ones). This is estimated as the ultimate weightage, Wi. Then the % age loss of weight of tablets was computed by utilizing the equation given under [13].

\[
\text{Percentage friability}= \left(\frac{\text{wi}-\text{wf}}{\text{wi}}\right)\times 100
\]

RESULTS AND DISCUSSION

Label information of tablet brands
The Label known information about all brands are listed in table 1.

Table 1: Labeling information regarding samples

| B # code | B # No | Pr. (10) Tabs. | Mfg Date | Exp Date | Manufacturer |
|----------|--------|----------------|----------|----------|--------------|
| Mecobal  | 129890 | 168            | Mar-2019 | Feb-2022 | Hilton Pharma |
| Cobalamin| 9006   | 96.51          | Apr-2019 | Apr-2024 | Macter International |
| Neumert  | Q596   | 133.90         | Feb-2020 | Feb-2023 | Martin Dow Marker |
| Incobal  | 444    | 78.08          | Feb-2019 | Feb-2022 | Indus Pharma |
| Qbal     | 19692  | 64.09          | May-19   | Apr-22   | Bosch Pharmaceuticals |
| Mecobal  | 003    | 82.69          | Feb-19   | Feb-22   | Nabiqasim Industries |

*Abbreviations: B # No (Batch Number), Pr. (Price), Mfg (Manufacturing Date), Exp (Expiry Date), of the total batches (n=3).

Table 2: Physical manifestations of various brands

| B-Code  | Color | Coating     |
|---------|-------|-------------|
| Mecobal | White | Sugar Coated|
| Cobalamin| White | Sugar Coated|
| Neumert | White | Sugar Coated|
| Incobal | White | Sugar Coated|
| Qbal    | White | Sugar Coated|
| Mecobal | White | Sugar Coated|

*Abbreviation: B-code (Batch code), of the total n=3 all batches show same color and coating.
Weight uniformity of tablet samples

All the selected tablet brands were within the weight variation specified limits except Mecobal with a relative standard deviation over 6.83% as affirmed in table 3.

Thickness of various tablet brands

The average thickness of Cobalamin, Incobal, and Mecobal were not within limits of standard specifications as revealed in table 4.

Hardness of tablet brands

The average hardness of all brands was within the limits except Cobalamin (10.49 kp) and Mecobal (10.462 kp) above 6kp as described below in table 5.

Stability studies of tablet brands

Stability of a biopharmaceutical product can be described as the capacitance of a specific preparation in a definite container/closure system to persist within its physical, chemical, microbiological, hazardous, defensive and informational specifications [16]. The objective of stability is to offer substantiation on how the superiority of a formulation differs with time under the effect of a diversity of environmental aspects like temperature, moisture, and light. Dilapidation is probably to arise under steamy environment of higher ambient temperature and humidity [17]. Therapeutic product stability is a multifarious
collective procedure which needs substantial time, expenditure, utilization, and methodical skills to synthesize therapeutically efficient formulations, efficiency, excellence and safe nature [18].

The results of accelerated stability at 3 temperatures, lab temperature, 30 °C±65% and 40 °C±75% respectively for a duration of 3 mo were within the specified limits as revealed in table 8.

### Table 8: Stability studies of chosen brands

| Brands     | Conditions | Stability Results |
|------------|------------|-------------------|
| Methycobal | 25 °C      | 99.13%            |
|            | 30 °C±65%  | 98.16%            |
| Cobalamin  | 40 °C±75%  | 90.02%            |
|            | 25 °C      | 93.03%            |
|            | 30 °C±65%  | 93.86%            |
|            | 40 °C±75%  | 93.39%            |
| Neuromet   | 25 °C      | 101.02%           |
|            | 30 °C±65%  | 101.72%           |
|            | 40 °C±75%  | 100.33%           |
| Incobal    | 25 °C      | 111.03%           |
|            | 30 °C±65%  | 111.94%           |
|            | 40 °C±75%  | 109.71%           |
| Qbal       | 25 °C      | 96.51%            |
|            | 30 °C±65%  | 96.88%            |
|            | 40 °C±75%  | 97.32%            |
|            | 25 °C      | 93.71%            |
| Mecobal    | 30 °C±65%  | 94.85%            |
|            | 40 °C±75%  | 94.32%            |

Total (n=3) showed stability results at temp 25 °C, 30 °C±65% RH (Relative Humidity) and 40 °C±75% RH (Relative Humidity).

### HPLC sampling results and calculations

The photosensitive material, mecobalamin, emerges at retention time of approximately 3.68 min. Usual changing in the chromatography scheme can essentially cause changeable investigational surroundings. The endeavor of this measurement is to uphold a constant extrication performance. The chromatogram retention time is given in fig. 2.

The results of HPLC of tablet brands are mentioned in table 9 and calculations are given underneath the table 9.

![Chromatogram](<image>)

**Fig. 2: HPLC results chromatogram of mecobalamin retention time 3.64**

### Table 9: HPLC facts about different brands

| Product-B | B. No | Conditions | Mcg/Tablet Result |
|-----------|-------|------------|-------------------|
| Methycobal| 129890| 30 °C±65%40 °C±75% | 490.78490.12 | 98.16%98.02% |
| Cobalamin | 9006  | 30 °C±65%40 °C±75% | 469.29466.96 | 93.86%92.39% |
|            | 30 °C±65%40 °C±75% | 508.58501.67 | 93.86%92.39% |
|            | 30 °C±65%40 °C±75% | 559.72548.57 | 93.86%92.39% |
| Neuromet   | Q596  | 30 °C±65%40 °C±75% | 483.34477.23 | 97.88%92.32% |
|            | 30 °C±65%40 °C±75% | 474.26471.62 | 94.85%94.32% |

*Abbreviations: B. No (Batch number), Mcg (Microgram) at temp 25 °C30 °C±65% RH (Relative Humidity) and 40 °C±75% RH (Relative Humidity) = Results*
CONCLUSION
It was noticed that a larger discrepancy in worth in the identical generic brands of Methylcobalamin. Qbal with cost 64.09 Pakistani rupees/ten tablets was observed commercially efficient. Nevertheless, as per the consequences of present readings disclosed no significant diversity in the qualitative analysis of Methylcobalamin brands. The superiority in stipulations of weight, thickness, disintegration, Friability and chemical evaluation (HPLC) were appraised, compared and found equivalent to one and other. Stability testing indicated every brand is comparable to other. Consequently, this is demonstrating that less rated medicines also offer excellent biopharmaceutical beneficial outcomes. Hence, it was summed up that the worth effectual drug ought be employed and may be recommended.

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CONFLICT OF INTERESTS
The Author of this article has no conflict of interest.

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