

CYCLIC VOLTAMMETRIC STUDY OF LOSARTAN POTASSIUM

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ABSTRACT

Losartan Potassium is antihypertensive drug which has a significant role in lowering blood pressure. In present study different electrochemical parameters such as E_p , $E_{p/2}$, α (transfer coefficient) were determined at different scan rates in Britton Robinson buffer. Moreover, the different pH and concentration of analyte and its influences on repeated scans were also studied by using gold disc electrode Vs saturated calomel (SCE) reference electrode at $30 \pm 1^\circ \text{C}$. Voltammograms of losartan potassium showed that two electron transfer reduction process was significantly altered by changing pH. The method was validated both for qualitative and quantitative determination of losartan Potassium.

KEY WORD:

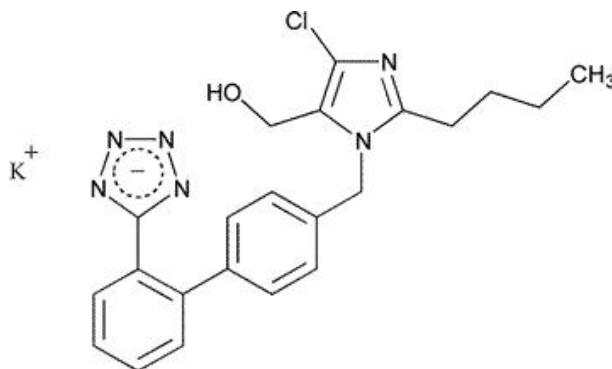
Cyclic voltammetry, Losartan Potassium, Electrochemical parameters, Transfer coefficient, gold electrode.

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1.0 INTRODUCTION:

Losartan potassium belongs to class I antihypertensive agent [3]. It is effectively used for the treatment of moderate or severe hypertension and heart disease either singly or some time with diuretics [1,2]. Losartan potassium is very selective, nonpeptide angiotensin II receptor antagonistic [1]. The dosage of losartan potassium increases the plasma rennin activity which causes elimination of angiotensin II feedback [1]. It is also used for the protection of type II diabetic disease for patients with proteinuria and stroke prevention.

Losartan potassium is a white crystalline fine powder, soluble in aqueous medium which is metabolized in liver. The I.U.P.A.C name of losartan potassium is (monopotassium salt) 4-butyl -4-chloro-1-[[2 - (1 H- tetrazol-5-yl) [1, 1'- biphenyl] -4-yl]methyl] - 1H -imidazole -5- methanol [5-9], with the following structure.



Losartan potassium

Literature reveals that several analytical methods have been used for the qualitative studies of losartan potassium like high performance liquid chromatography (HPLC), high performance thin layer chromatography (HPTLC) and electrochemical radioimmunoassay. The simultaneous estimation by first order derivative spectroscopy [5] and Hydrochlorothiazide (HCT) [13-15] were used to study singly and in combination with hypertensive diuretics drugs. The reverse phase high pressure liquid chromatography (RP- HPLC), and thin layer chromatography method [5] including spectrophotometric determination and cathodic stripping voltammetry (using dropping mercury electrode) have also been carried out in acidic medium. However no cyclic voltammetry has yet been reported so far in the literature on losartan potassium.

In the present work cyclic voltammetry was performed at **gold electrode** for the determination of electrochemical parameters of losartan potassium

This technique has been used due to its sensitivity and selectivity. It is versatile technique which is used for method validation, as well as for quantitative and qualitative measurement of the pharmaceutical significant compounds.

2.0 EXPERIMENTAL:

CHI- 700 Cyclic Voltammeter was used for recording voltammograms of the analyte using **gold as working electrode** V/S Hg/Hg₂Cl₂ electrode as reference electrode and Platinum (Pt) were used as counter electrode. A pH- meter (Jenvay) was also used

for monitoring the pH of supporting electrolytes and conductivity meter HANNA (HI- 8633) (Romania) used to measure the conductivity.

2.1 REAGENTS:

Britton Robinson buffer (Laboratory prepared) was used as a supporting electrolyte comprising boric acid, acetic acid, and phosphoric acid. A Stock solution of Losartan potassium of 3×10^{-3} mole/dm³ (E. Merck) was prepared in 0.04M Britton Robinson Buffer. All reagents used were of analytical grade and were prepared in double distilled water.

2.2 GENERAL PROCEDURE:

The solution (10 ml) of losartan potassium (3mM) was filled in electrochemical cell which was connected with the three electrodes gold as working electrode, platinum as counter and Hg/Hg₂Cl₂ as reference electrode with potentiostat. Argon gas (99.99%) pure was purged for 20 min for inert atmosphere. The voltammograms of the analyte were recorded at $30 \pm 1^\circ\text{C}$. To avoid the contamination of the surface of gold test electrode, it was renewed with polishing material and washed several times with distilled water and drying with watman filter paper.

The parameters like initial and final potential and the scan rates were adjusted before taking the voltammograms of sample. Base line of supporting electrolyte has been run initially which was horizontally straight and finally the voltammograms were recorded.

3.0 RESULT AND DISCUSSIONS:

In present study as the qualitative analysis of losartan potassium was performed in Britton Robinson buffer in basic medium pH- range (8-11). Voltammograms of losartan potassium were taken at different scan rates ranging from 20-500mV/s at gold electrode in negative potential range (0 -1.0 mV/S) as shown in figure 1. The first reduction peak was appeared at -0.552 V (with cathodic peak current 1.101×10^{-6} μA) and second peak at -0.828mV/S (with cathodic peak current 1.739×10^{-6} μA). A third peak was also appeared on reverse scan at (300-500) mV/S in pH 11.

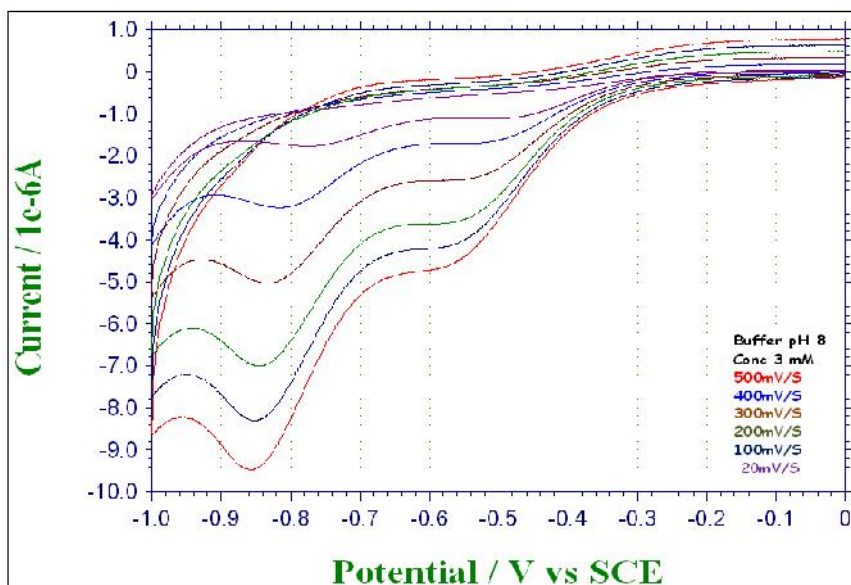
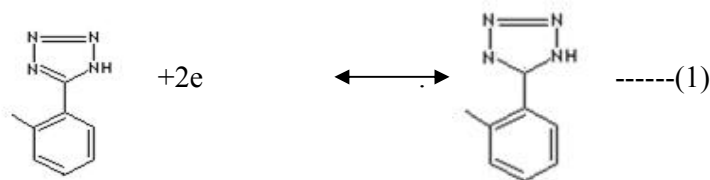


Figure 1: First scan cyclic voltammograms of 3mM losartan potassium at gold electrode Vs SCE reference electrode with different scan rates in presence of Britton Robinson buffer at pH 8 at 30±1°C.

3.1 REACTION MECHANISM:

The structure of losartan potassium molecule contains imidazole group and tetrazolyl group. These functional groups do not easily reduce electrochemically while by providing potential to the gold electrode in aqueous medium it can be reduced [17]. At high pH >7 analyte can be reduced at the surface of working electrode due to the presence of halide group [18]. The possible mechanism of electrode reaction carried out on the surface of the test electrode can be assigned to proton transfer reaction which is actually coupled to electron transfer hence reduces azomethane group C=N in tetrazolyl group into saturated bond involving two electrons and two protons. This is also confirmed by the present voltammograms of losartan potassium where two waves appeared due to the two electrons transfer process. The similar observation has also been reported [17]. and represented in equation 1. By applying the diagnostic test of catalytic mechanism and compare with the experimental result of losartan potassium it fulfills the diagnostic test of catalytic reaction mechanism [16].



3.1.2 EFFECT OF SCAN RATE:

A linear trend was observed between the reduction peak currents (I_{pc}^1 & I_{pc}^2) and the square root of the scan rates which confirms that this is a diffusion controlled process [17] which is shown in Fig 2. The Value of r^2 (0.994) statistically representing the strong relationship between I_{pc}^1 V/s $u^{1/2}$. The second reduction peak current also showed a linear pattern I_{pc}^2 V/s $u^{1/2}$. The possibility of irreversible process the value E_p^c shifts towards negative potential range [16]. In present case the same trend was obtained in the voltammograms of losartan potassium at different scan rates (20, 100,200,300,400,500 mV/S), which is shown in figure 2 and table No.1. The values of transfer coefficient α were calculated by using equation 2. According to Bard and Faulkner α can be calculated by the following equation no 2.

$$\alpha = 47.7 / (E_{pc} - E_{p/2}) \quad \text{-----(2)}$$

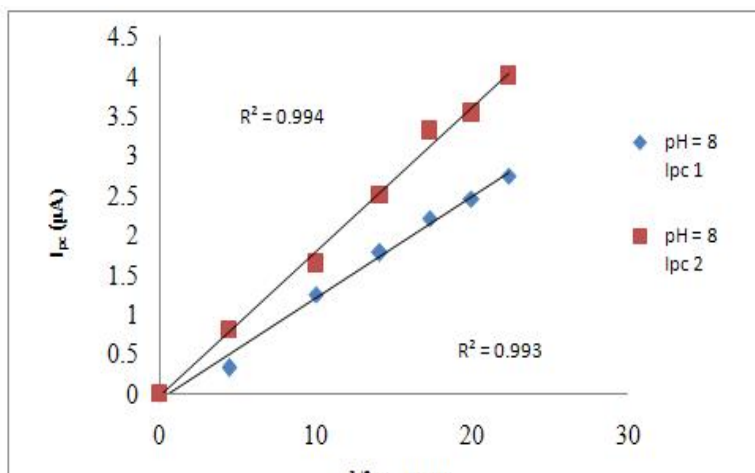


Figure: 2 The plot of I_{pc}^1 and I_{pc}^2 Vs $u^{1/2}$ in Britton Robinson buffer (pH=8) at $30 \pm 1^\circ\text{C}$.

3.1.2 EFFECT OF CONCENTRATION:

The effect of concentration of analyte on peak current was also studied in 0.04 M Britton Robinson buffer in basic pH range from (8-11). In present study Britton Robinson buffer was used as a supporting electrolyte. The values of E_{pc}^1 and E_{pc}^2 are found to be independent with change in concentrations range (1×10^{-3} to 3.5×10^{-3} M) of analyte at 100mV/S scan rate. The Value of I_p^c Vs concentration range (1×10^{-3} - 3.5×10^{-3} M) of analyte passed through origin confirmed that this is diffusion controlled process, which is shown in figure 3. The repeated scan rates of 3mM losartan potassium at 100 mV/S showed that product adsorption occurred in terms of reduction of proton at a gold electrode surface as compared to adsorption and desorption of hydrogen ion explained by Greef et al (1985). [16].

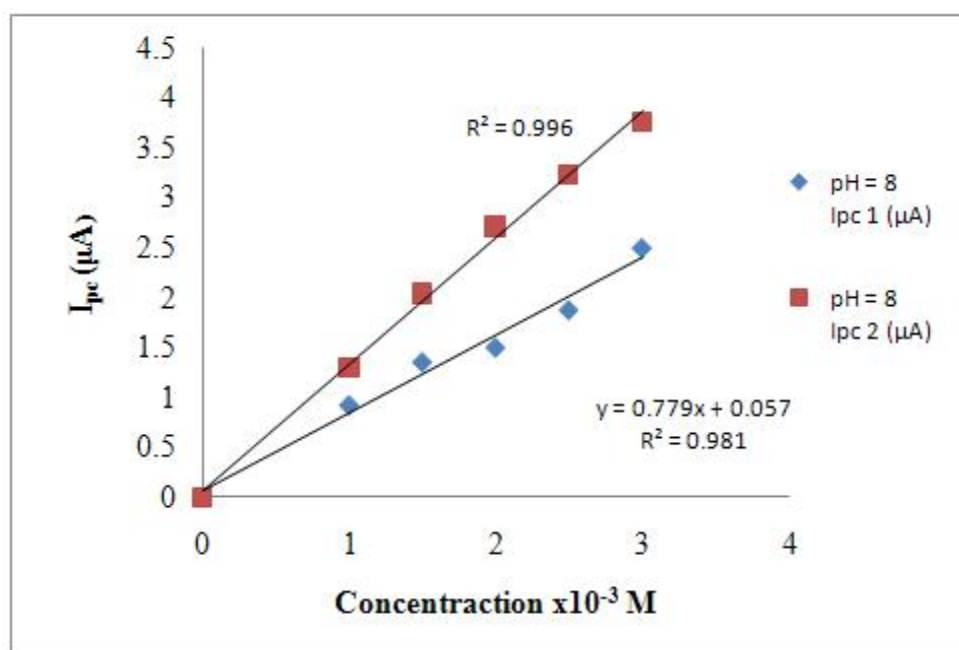


Figure: 3 The plot of I_{pc}^1 and I_{pc}^2 Vs concentration of losartan potassium at 100mV/S in Britton Robinson buffer at $30 \pm 1^\circ\text{C}$.

3.1.3 EFFECT OF PH:

Voltammograms of 3mM of losartan potassium were taken at different pH of Britton Robinson buffer at 100mV/S scan rate which is shown in fig 4. An insignificant change was found in peak potential (E_{pc}^1 and E_{pc}^2) with the increase in pH of Britton Robinson buffer, on the other hand a significant decrease in I_{pc}^1 & I_{pc}^2 was observed at 100mV/S with a increase in pH from 8-11 which is shown in fig 5. The variation in peak height, peak current and peak potential was observed which is shown in fig 4. Peak

potential (E_p°) by changing the pH explained that low conc. of analyte is available for reduction on the surface of gold disc electrode. This is possibly due to the slow diffusion process of analytes from the bulk to the test electrode surface at high pH range as compare at low pH which was also reported earlier [16].

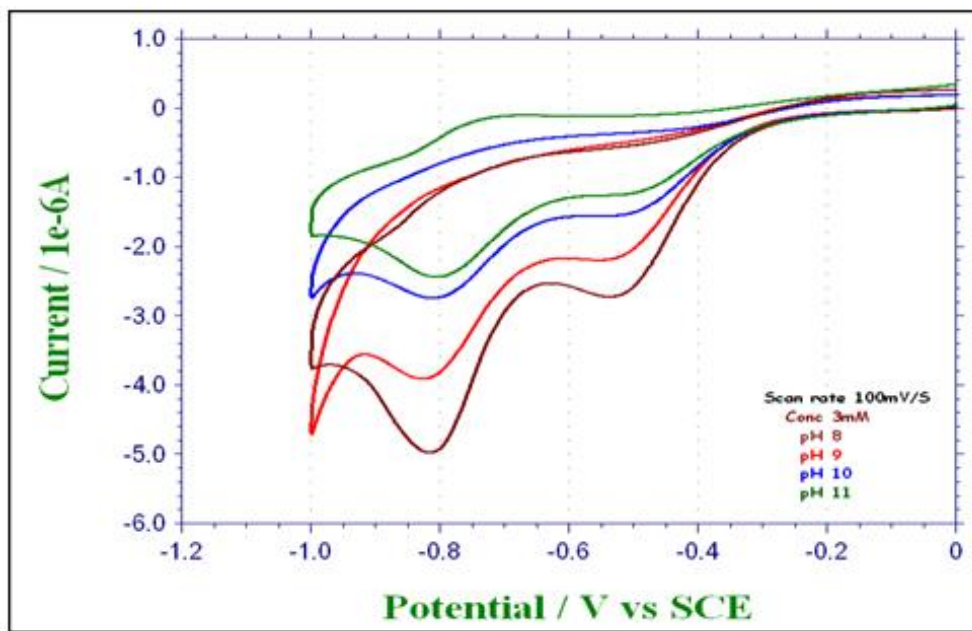


Figure 4: Cyclic voltammograms of 3mM losartan potassium at gold electrode Vs SCE reference electrode 100mV/S scan rate in Britton Robinson buffer pH (8-11) used as supporting electrolytes at $30\pm 1^\circ\text{C}$.

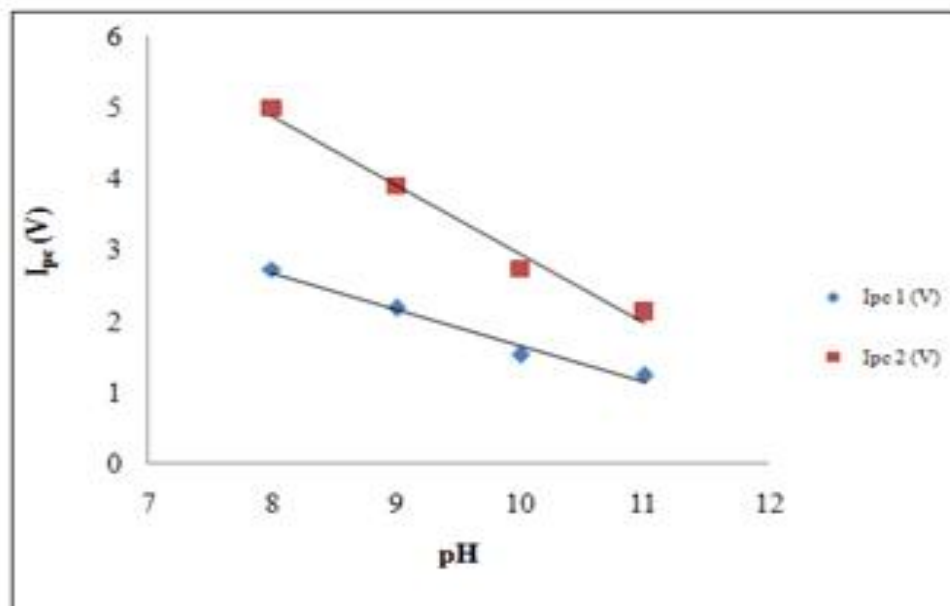


Figure 5 The plot of I_{pc}^1 and I_{pc}^2 Vs of pH of Britton Robinson Buffer at 100mV/S scan rate at $30\pm 1^\circ$

3.1.4 DIAGNOSTIC TEST FOR REVERSIBILITY:

The reported diagnostic tests for reversibility were applied to confirm the characterization of losartan potassium in Britton Robinson buffer system in different pH range (8-11). It partially fulfilled the diagnostic test of quasi reversible systems [16]. The criteria for a quasi reversible process is that the I_p^c values increase with the increase in $u^{1/2}$ but not proportional to it but in case of losartan potassium I_p^c values are directly proportion to the square root of the scan rates. Secondly the ratio of I_p^a/I_p^c should be "1" provided $\alpha_a = \alpha_c = 0.5$. In case of losartan potassium the ratio of I_p^a/I_p^c is < 1 within the limits of experimental error as briefly explained by Greef et al (1985). Thirdly ΔE_p is greater than $59/n$ mV and increases with increasing scan rates. But in case of losartan potassium at low scan rate ΔE_p was found to be lesser than $59/n$ mV and at high scan rates ΔE_p values $> 59/n$ mV and increases with rate of potential scan by Renmuth (1962) and Bard & Flukner (1980). Finally the peak potential was shifted cathodically by increasing the scan rates according to the criteria of quasi reversible process.

3.1.5 DIAGNOSTIC TEST FOR IRREVERSIBILITY:

CV profile of losartan potassium at pH 8 and 9, at low scan rate follow the criteria of irreversibility. No reverse peak should appear while in case of losartan potassium at low scan rates no reverse peak obtained. Secondly, I_p^c directly proportional to the square root of scan rates but in present work a linear trend was also found in cathodic current with the increase in the square root of scan rates. Third criteria of irreversibility should be E_p^c shifts $-30/\alpha_a n_\alpha$ for each decades mean while the same pattern was observed in C.V. profile of losartan potassium. Finally, the difference of $|E_p^c - E_{p/2}^c|$ should be equal to $48/\infty_c n_\alpha$ but in case of losartan potassium the difference of $|E_p^c - E_{p/2}^c|$ was found to be greater than $48/\infty_c n_\alpha$. In case of losartan potassium almost full fills the criteria of irreversibility [16].

4.0 CONCLUSION:

It was finally concluded that the CV profiles of losartan potassium was performed at gold as working electrode Vs saturated calomel electrode $Hg|Hg_2Cl_2$ as reference electrode at $30 \pm 1^\circ C$ showed two electron transfer process. It fulfills the diagnostic test of irreversible process and it follows the catalytic reaction mechanism. Base line was found to be horizontally straight. The qualitative and quantitative characteristics of losartan potassium were studied in 0.04 M Britton Robinson buffer which was used as supporting electrolytes where E_p^c , $E_{p/2}$, D (diffusion coefficient), and α (transfer coefficients) were determined at different scan rate at pH (8-11) which is shown in table 2. This technique is also used for the method validation of pharmaceutical compounds/ drugs

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Table1: The value of E_{pc}^1 & E_{pc}^2 and I_{pc}^1 & I_{pc}^2 from the cyclic voltammogram of Losartan potassium 3×10^{-3} mole /dm³ in Britton Robinson buffer (pH =8) used as supporting electrolytes with different scan rates at 30°C.

Peak ¹					
Scan rates (mV/S)	E_{pc}^1 (mV/S)	$E_{p/2}$ mV/S)	$E_p-E_{p/2}$ (mV/S)	$\alpha = 48/E_p-E_{p/2}$	$I_{pc}^1 \times 10^6$ (μA)
20	503.5±2.94	430.7±1.15	72.73±2.57	0.66±0.02	0.93±0.01
100	532.2±0.53	456.23±0.06	75.97±0.59	0.63±0.00	1.77±0.01
200	552.73±0.06	452±0.61	100.73±0.59	0.47±0.00	2.562±0.02
300	577.2±0.10	462.8±0.10	114.4±0.17	0.42±0.00	3.61±0.01
400	586.93±0.06	470.63±0.51	116.3±0.46	0.41±0.00	4.23±0.04
500	595.2±0.10	472.4±0.10	122.8±0.20	0.40±0.00	4.67±0.01
Peak ²					
Scan rates (mV/S)	E_{pc}^2	$E_{p/2}$	$E_{pc}-E_{p/2}$	$\alpha = 48/E_{pc}-E_{p/2}$	$I_{pc}^2 \times 10^6$ (μA)
20	798.1±0.09	704.4±0.11	93.6±0.05	0.512±0.00	0.621±0.00
100	818.8±0.53	737.2±0.12	81.5±0.64	0.58±0.00	1.542±0.00
200	834.1±0.10	743.63±0.06	90.46±0.15	0.53±0.00	2.104±0.01
300	843.1±0.10	753.6±0.10	89.5±0.10	0.54±0.00	3.318±0.00
400	847.1±0.06	761.5±0.26	85.67±0.31	0.56±0.00	3.87±0.01
500	856.1±0.06	768.2±0.10	87.967±0.15	0.55±0.00	4.242±0.00

Table 2: values of α , Diffusion coefficient, R^2 and Slope of I_{pc}^1 of 3mM of losartan potassium at different pH of Britton Robinson buffer at 100mV/S.

Peak ¹					
S.No	pH	α	“D” (cm ² /s) 10 ⁵	Slope “m” 10 ⁻⁶	R^2
1	8	0.637±0.001	0.8705±0.01	0.174±0.01	0.999±0.01
2	9	0.630±0.02	0.1295±0.01	0.246±0.01	0.962±0.01
3	10	0.515±0.02	0.1887±0.01	0.224±0.01	0.987±0.02
4	11	0.654±0.01	0.1882±0.01	0.148±0.01	0.980±0.02
Peak ²					
S.No	pH	α	“D ^{1/2} ” (cm ² /s) 10 ⁵	Slope “m” 10 ⁻⁶	R^2
1	8	0.585±0.01	1.133±0.01	0.208±0.01	0.997±0.01
2	9	0.625±0.02	2.051±0.015	0.561±0.01	0.993±0.01
3	10	0.782±0.015	3.438±0.021	0.542±0.01	0.994±0.12
4	11	0.8421±0.01	0.955±0.01	0.339±0.12	0.987±0.01

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