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MADRAS RECORD OFFICE.

Government of Madras.

Revenue **DEPARTMENT.**

G.O. No. 652 Press ~~Mis~~

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Dated 19 — 3 — ~~19~~ 1857

Not to be folded or roughly handled

Proceedings of the Madras Government, Revenue Department,
19th March 1867.

Read the following papers :—

No. 302. From the President and Members of the Chinchona Commission, to the Secretary to Government, Revenue Department, Fort Saint George, dated Madras, 28th February 1867.

1. With reference to the Order of Government, as per margin, we have the honor to report that the printing of the tabulated results of the experimental use of Chinchona Alkaloids has occasioned some delay in the submission of a progress report. A considerable number of the tables, however, have now been printed, so as to enable us to estimate, with tolerable precision, the therapeutical effects of the several alkaloids ; and, as our President will have no other opportunity of recording his views as to the usefulness of these medicines, the Members of the Commission have decided to conclude now a preliminary report of their proceedings, leaving their more detailed observations to follow when the results of the experiments still in progress are more fully known.

No. 764 of 28th March 1866.

2. In the Tabular Statements, already printed and laid before the Commission, minute particulars in regard to 1,145 cases of paroxysmal fevers treated either by Chinchonine, Chinchonidine, or Quinidine, have been registered. These fevers have occurred mostly at stations notedly malarious, such as at Goodaloor in the Wynaad ; Sumblepoor and Russelcondah in the Northern Circars ; the Godavery jungles ; Mysore, Cochin, and Labuan, and may, therefore, be regarded as fair average types of the forms of paroxysmal fever to be met with in the malarious districts of Southern India.

3. A larger number of cases have been treated up to date, but the Returns have not yet been received, or, if received, are not out of the printer's hands, so that the results must be considered in detail hereafter.

4. With regard to the 1,145 cases of fever referred to, it will suffice to note that they were treated by the alkaloids, as follows :—

By sulphate of	Chinchonine	410
Do.	Chinchonidine	359
Do.	Quinidine	376

The doses and mode of administration varied a good deal. Some Medical Officers used large doses of from 15 to 20 grains ; others, medium doses of from 8 to 10 grains, and some small doses of from 2 to 5 grains. As a general rule, the Members of the Commission are of opinion that the experiments were most successful when medium doses were employed, that is, the cases of fever in which 8 or 10 grains of alkaloid were administered in a single dose daily, appeared to recover more expeditiously than where larger or smaller quantities were employed. Large doses of Chinchonine, Chinchonidine, and Quinidine produce effects very similar to those of Quinine. Disagreeable noises in the head, singing in the ears, deafness, and giddiness are the more noticeable of the symptoms produced by all of the Chinchona alkaloids. Vomitting, nausea, and purging also are occasionally noted to follow their use. On the other hand, small or moderate doses produce none of

these peculiar effects, while they improve the appetite, strengthen the digestion, and, in many cases, appear to have a marked effect in reducing the size of congested spleens.

5. The alkaloids were exhibited successfully, that is, with the result of a rapid cessation of febrile paroxysms in a very large proportion of the cases. Out of the 1,145 cases recorded, four deaths occurred, and all these took place at Goodaloor, in Wynaad. Dr. Keess observes of them, that the fever was complicated either with Pneumonia or Diarrhœa, and that a great proportion of his patients were half-starved, emaciated persons, completely prostrated by the malarious influences surrounding them.

In addition to the cases ending fatally, it is recorded that the alkaloids failed more or less to arrest febrile paroxysms in twenty-seven persons—a proportion a little in excess of two per cent. of the total cases treated.

6. In regard to these failures, it must be noted that they occurred chiefly in the practice of gentlemen who tried the alkaloids, not in recent attacks of fever, but in patients whose systems were chronically poisoned by malaria. Thus, Mr. Walters, of the 4th Regiment N. I., Secunderabad, records of many of his cases, that they had been from one to three or four months suffering from fever before he used the alkaloids, and that in some of them Quinine failed just as much as Quinidine, Chinchonine, or Chinchonidine had done. Mr. Chipperfield explains the probable cause of failure in his Report (Appendix III). In recent attacks of uncomplicated paroxysmal fever, the new alkaloids appeared to most of the Medical Officers using them, and to the Members of the Commission, to be quite as efficacious in the curing of fevers, as Quinine. On this subject, however, it is impossible to speak with precision, until the results of treatment with the chemically pure di-sulphate of Quinine, as supplied by Messrs. Howards, have been tabulated in the form used for recording the treatment by the other alkaloids. Instructions have been issued to the gentlemen engaged in the experiment to do this, and the returns, when received, will afford most valuable data whereby to compare the relative therapeutical effects of the several alkaloids.

7. The evidence, so far as it has come before the Commission, does not go to shew any particular superiority of one alkaloid over another.

The sulphate of Quinidine is, perhaps, the one regarding which there is the least difference of opinion as to its merits. All three are undoubtedly anti-periodic, and capable of controlling paroxysmal fevers. The sulphate of Chinchonine in *large* doses perhaps causes more unpleasant symptoms than the others; but on this point further evidence is still wanting to enable the Commission to offer a positive opinion. As regards the general and practical question at issue, we agree with

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Dr. Keess in thinking that all three alkaloids are, equally with Quinine, capable of controlling paroxysmal fevers. Dr. Keess' experience led him to conclude that a 10-grain dose of either salt, would check or postpone the febrile paroxysm in a considerable number of cases, while very few patients required more than a second 10-grain dose to subdue the disease for the time being.

Other observers have employed larger quantities of the several drugs; but it is by no means clear to the Commission, that the quantities exhibited were, in all cases, necessary to check the fever. As regards this part of the inquiry, it is intended to institute a distinct series of experiments for the more accurate comparison of the value of the several alkaloids, when contrasted with Quinine, or with each other.

8. The main conclusion which the Members of the Commission have derived from the data before them, is that the alkaloids hitherto but little valued in medicine, are scarcely, if at all, inferior as therapeutical agents to Quinine.

What the exact differences may be in their physiological and therapeutical action, is a question the answering of which may fitly be deferred until more data have been collected in reference to the new alkaloids. The differences, however, will most likely be found to be of degree, rather than of kind, and practically, so far as the wants of India are concerned, it will be just as well that the locally grown barks yield a large proportion of one alkaloid as of another.

9. So impressed are we of the value of these hitherto despised alkaloids, that the Members of the Commission are unanimous in considering that, in the public service of this country, they may very advantageously be substituted in part for Quinine. If three pounds of Chinchonine can be obtained at the price of one pound of Quinine, we consider that a great public good would result from the purchase of the larger quantity, as it would enable the Officers of the Medical Department to benefit a much larger number of the population than they can now afford to treat by prescribing Quinine. Arrangements will be made by Dr. Mackenzie to include in the next Medical Indent on the Home Government a requisition for suitable quantities of each alkaloid.

10. We beg to direct attention to the tables, &c., in the Appendix. It gives us much pleasure in testifying that the experiments conducted by Dr. Keess at Goodaloor have been most carefully recorded.

11. Mr. Cornish, Secretary to the Principal Inspector General, in addition to his other duties, voluntarily undertook those of Secretary to the Commission. For the mode in which these duties have been carried out, the Members of the Commission feel that their best acknowledgments are due to that gentleman.

APPENDIX I.

TABLE 1.—*Shewing the results of treatment of paroxysmal fevers by Chinchonine.*

	Name of Medical Officer.	District.	Type of Fever.			Results.		Remarks.
			Quotidian.	Tertian.	Remittent.	Cured.	Failed.	
1	Dr. Keess and Mr. Wade.	Goodaloor (Wynaad) ...	170	19	1	188	2*	Large doses produced disagreeable effects; usual dose from 5 to 10 grains daily. Dr. Keess considers the remedy equal to Quinine.
2	,, Foy	Sumbulpore	31	6	1	38	...	Chiefly 5-grain doses from two to three times daily.
3	,, Cleveland	Mysore...	38	4	2	43	1†	Dose grains v—xx three times a day. Chinchonism resulted when large doses were given.
4	,, Whitton	Cochin...	25	3	...	28	...	Single dose of 10 grains in a few. In most 5 grains before expected paroxysm. Remedy appeared to effect rapid reduction of size of spleen in several cases.
5	,, White, 1st Royals ...	Kamptee	6	...	...	6	...	Small doses of 2 or 3 grains used. Had larger doses been given, the cure would have been more rapid.
6	,, Dougall	Northern Circars ...	18	2	...	16	...	Given in v, x, and xv grain doses.
7	,, Chipperfield	Madras...	8	2	1 Contd.	8	3*	In unsuccessful cases the remedy was not continued more than two days, small doses only given.
8	,, Heard	Shemogah, Mysore ...	2	...	...	2	...	
9	,, Walters	Secunderabad	18	3	...	17	4	Nearly all Dr. Walters' cases had been a long time under other treatment before Chinchonine was resorted to. They were obstinate intermittents, and did not yield readily to treatment. Many of the cases had "burning of the hands and feet."
10	,, Fitzgerald	Labuan	14	5	...	19	...	Small doses used which rendered treatment protracted.
11	,, Houston	Upper Godavery ...	35	...	...	35	...	Chinchonism resulted when repeated large doses were used. Dr. Houston notes that, in the majority of cases, the pulse rose soon after taking a dose of the medicine.
			361	44	5	400	10	
		Total...	410			410		

* Both died from exhaustion.

† Complicated with pneumonia—the remedy was discontinued.

TABLE 2—Shewing the results of treatment of paroxysmal fevers by Chinchonidine.

	Name of Medical Officer.	District.	Type of Fever.			Results.		Remarks.
			Quotidian.	Tertian	Remittent.	Cured.	Failed.	
1	Dr. Keess and Mr. Wade...	Goodaloor	137	16	1	154	...	These cases were nearly all cured by from one to two doses of 8 or 10 grains.
2	,, Foy	Sumbulpore ...	36	5	...	39	2	In the cases of failure Quinine was resorted to, but the result is not stated—generally used in 5-grain doses.
3	,, Cleveland	Mysore	24	10	4	38	...	Doses varied from v to xx grains—small doses in a few cases with less immediate effect.
4	,, Whitton	Cochin	28	4	...	31	* 1	
5	,, White, 1st Royals ...	Kamptee	...	...	...	...	...	
6	,, Dougall	Northern Circars ...	12	3	...	15	...	Given in v, x, and xv grain doses, considered by Dr. Dougall quite equal to Quinine.
7	,, Chipperfield... ...	Madras	8	3	1	7	5	Three of the unsuccessful cases were only one day under treatment. See Dr. Chipperfield's remarks in Appendix III.
8	,, Heard	Shemogah, Mysore ...	11	...	...	10	1	Grains 8 to 10 before paroxysm.
9	,, Walters	Secunderabad ...	7	1	...	5	3	As regards three cases the results are so vaguely given, that it cannot be said whether the remedy failed or not.
10	,, Fitzgerald	Labuan	18	4	...	22	...	Grains 3, 6, 8, before paroxysm.
11	,, Houston	Upper Godavery ...	25	1	...	25	† 1	
			306	47	6	346	13	Three doubtful.
		Total...	359			359		

* Fever became remittent.

† Complicated with Neuralgia and Paralysis.

Table 3.—*Shewing the results of treatment of paroxysmal fevers by Quinidine.*

	Name of Medical Officer.	District.	Type of Fever.		Results.		Remarks.
			Quotidian.	Tertian.	Remittents.	Cured.	Failed.	
1	Dr. Keess and Mr. Wade...	Goodaloor	140	11	2	151	2	Both died, one from exhaustion, one dysentery.
2	,, Fry	Sundahpore	37	6	...	43	1	Chiefly 5-grain doses, three times a day.
3	,, Cleveland ...	Mysore	28	5	...	33	...	2 cases result not known. From 2 to 20 grain doses, 3 times daily.
4	,, Whitton	Coorg	26	3	...	29	...	Chiefly 5-grain doses. In a few cases 10 grains.
5	,, White, 1st Royals ...	Kamptee	9	...	...	9	...	3 and 5-grain doses, three times daily.
6	,, Boswall	Northern Circars ...	11	4	...	14	1*	5, 12, and 15 grain doses.
7	,, Chipperfield ...	Madras	8	...	...	8	...	5-grain doses, thrice daily.
8	,, Heard	Shemgodi, Mysore ...	12	...	2	12	2†	Doses 2, 4, 5, and 6 grains.
9	,, Walkers	Secunderabad	15	1	...	14	2	Some of the cases were successfully treated, hypodermically. The two failures cured by Quinine.
10	,, Fitzgerald	Lahore	9	1	...	10	...	6-grain doses.
11	,, Houston	Upper Godavery... ...	10	1	1	12	...	Grains v to x, twice a day.
12	,, Henderson	Bangalore... ...	15	...	...	13	3‡	Grains v to x, chiefly in interval of fever.
13	,, Oswald	Do.	17	2	...	19	...	
	Total...		337	34	3	365	11	
			376			376		

* In this case paroxysm only mitigated not checked.
† These were cases of remittent fever, and remained under treatment though benefited.
‡ Remedy omitted on account of diarrhœa.

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APPENDIX II.

Report on the Chinchona Alkaloids.

1. In obedience to instructions received from the Head of the Medical Department, I proceeded to Goodaloor, south-east Wynaad, and started the alkaloids experiment on the 1st June 1866.

2. When I arrived at Goodaloor, fever was prevailing to a great extent, both there and in the adjoining coffee estates. Owing to the great rush of fever subjects to the Dispensary, I decided on first observing the effects of large doses of the alkaloids.

3. As there were many persons suffering from fever in June, the administration of a single large dose enabled me to take up a larger number of cases, than I would have been able to do, had I begun with small and repeated doses.

4. I first tried Chinchonidine, in doses varying from 10 to 15 grains, and, in a few days, I was pleased to find that it acted as Quinine would have done in similar doses.

5. I next tried Quinidine with similar results.

6. I left Chinchonine to the last, as it was said to be an irritant of the gastro-intestinal mucous surface. I was, however, agreeably disappointed, when I found that it did not cause nausea or vomiting in doses of 10 grains, and that it was as good an anti-periodic as the sister alkaloids.

7. Encouraged by the absence of symptoms indicating gastro-intestinal irritation, I used Chinchonine in fever complicated with diarrhœa, and I am satisfied that it is not an irritant of the stomach or bowels, any more than Quinine is, in certain cases.

8. Some of my patients were *out* and *in*-patients of the Goodaloor Dispensary. Others were visited in the bazaar, and in the adjoining coffee estates, from two to six miles distant from Goodaloor.

9. The great majority of my patients were half-starved, emaciated persons, with flabby muscles, dry, dirty, and shrivelled skins, large spleens, bloodless eyes and tongue, and small atonic pulse. In many of them, languor was so marked that they could, with difficulty, muster up energy enough to reply to questions; and so prostrated were some of them, that they were, with difficulty, induced to take the medicines offered to them.

10. I have not attempted to reduce, to a small compass, the results set forth in the tabular reports, as I hear that this work has been undertaken by the Chinchona Commission; but I beg leave to point out that a 10-grain dose, of all three alkaloids, seemed sufficient to check the return of fever in the majority of cases. Where it failed to check the return of fever, the succeeding paroxysm was generally observed to be less severe. When the paroxysms returned with unabated severity, 15 grains, and then 20 grains were tried. In a few severe cases, I administered, at the onset, 15 or 20 grains.

11. During the four months that I was employed in the Wynaad, 467 cases were treated with the alkaloids. The majority of these were cases of the quotidian type. Bronchitis, congestion of lungs, pneumonia, diarrhœa, dysentery, and anasarca were occasional complications. I may as well add, that these complications did not in the least interfere with the administration of the alkaloids. Where the local affection required special attention, the alkaloids were given with remedies suitable to the complication. I may here add that all three alkaloids appeared to be as efficacious as quinine.

* * * *

MADRAS,
25th February 1867.

(Signed) J. KEESS, M.D., Assistant Surgeon,
Late on special duty in the Wynaad.

APPENDIX III.

Report on the therapeutic effects of the Salts of the Chinchona Alkaloids.

1. In furnishing the accompanying tabular reports of the therapeutic effects of the Chinchona Alkaloids, as tested at the General Hospital, Madras, I have the honor to state, that in order to draw a more accurate comparison between the salts tested and the di-sulphate of Quinine, I exhibited the former in the same way as I am in the habit of using the latter, viz., I gave the first dose upon the decline of the sweating stage, the second and third doses being given at two-hour intervals. The fourth dose was exhibited at the same hour as the first dose, and so on with the fifth, sixth, and any subsequent doses which appeared to be required.

2. I have been led to form a high estimate of the anti-periodic effects of the sulphate of Quinidine. This salt was successful in the cure of the eight cases in which it was administered, and it appeared to me to be quite as valuable a remedy as the di-sulphate of Quinine itself. In some respects it seemed superior to Quinine, as in no instance did it produce any of the disagreeable effects termed Chinchonism; in fact, two patients who were suffering from severe headache, stated that the medicine completely relieved this symptom. I did not observe any injurious effects upon the digestive organs, but rather a favorable action, as appetite was promoted and digestion apparently assisted. In seven cases the Quinidine was given in doses of five grains thrice daily. As these doses were effectual, I continued them. But, as a matter of experiment, in case 8, I gave on the 11th of June, one dose of 15 grains on the decline of the sweating stage, and a second dose of 8 grains two hours before the next expected paroxsym. The patient was free from fever for five days, when a relapse occurred. The same plan of administration was followed and with success, for there was no further paroxysm of ague, although the patient remained under observation for Incipient Phthisis, for a period of more than a month.

3. The sulphate of Chinchonine I would place second on the list as an anti-periodic. It was unsuccessful in *three out of eleven cases*; but two of these were very unfavorable ones. One, a European Coffee Planter was suffering from Tœnia and general abdominal engorgement, and the remedy could not be pushed in his case, as it produced Chinchonism very rapidly. He had taken a large quantity of Quinine before the Chinchonine was commenced. He was subsequently treated with Pernitrate of Iron, Kuosso, Turpentine, and oil of Male Fern, but he did not pass the head or neck of the Tœnia, only a few proglottides. I saw him on September 17th very much improved in health, getting strong and stout, and quite free from fever. The second case, a European (Surgeon of the Ship "Blackwall,") was a relapse. Three weeks previously he had been cured of an intermittent by Quinidine. (Case 7 in the table.) He was then suffering from Chronic Hepatitis, and had threatenings of Hemiplegia. These symptoms quite disappeared before his first discharge from Hospital on the 19th June. On his second admission it was ascertained that he had been much exposed to the sun, going forwards and backwards among the shipping in the roads. The Chinchonine* failed to arrest the paroxysms of ague, which was subsequently effected by Quinine.

4. The third unsuccessful case was that of a Eurasian lad, whose stomach would not tolerate the remedy. He was subsequently cured by a combination of Diaphoretics with Quinine.

5. Gastric disturbance was produced by the Chinchonine in most of the successful cases.

6. The sulphate of Chinchonidine appears to me a much inferior anti-periodic to Quinine. It was unsuccessful in five out of twelve cases in which it was employed. I allowed myself to be somewhat prejudiced against the salt when I commenced its use, as it almost always produced nausea.

7. In Cases 1, 8, and 9, it was decidedly successful. Case 2 might be removed from the table; the man was saturated with malaria, and had previously been treated by Quinine and by Chinchonine.

8. Case 3 was a complicated one; the woman was the subject of Hysteria, and each cold stage was accompanied by violent hysterical fits. Her spleen was much enlarged, and, altogether, it was a most unfavorable case for even Quinine. Deobstruents were freely used, even whilst

* Only 3ss. given.

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taking the Chinchonidine. She is entered as having been successfully treated by the Chinchonine (Case No. 10 in the table). The fact is, there had been no paroxysm for two or three days whilst taking the Chinchonine, and as that salt was exhausted, she simply passed to the Chinchonidine. She has since had relapses, and has been treated by Quinine and Deobstruents. She was discharged at her own request on the 31st August, but since then has had a relapse and has again come under treatment.

9. Case 4 might be removed from the table; he had only one dose of Chinchonidine which increased mental delusions as Quinine had done before. He is still under treatment, occasionally getting a paroxysm of ague with very profuse sweating. He is improving under mineral acids, and his distressing mental delusions have disappeared.

10. In case 5, the remedy produced violent vomiting, and it was discontinued at the patient's request. The same remark may be made as to Case 6, subsequently cured by Quinine. Cases 7 and 12 were very mild cases, which would probably have been easily cured without any Chinchona preparation. In case 10, nine grains of Chinchonidine appeared to prevent the recurrence of a paroxysm. The patient, a very anæmic female, was subsequently cured by ferruginous remedies.

MADRAS, *18th September* 1866.

(Signed) W. N. CHIPPERFIELD, Assistant Surgeon,
Acting Physician, General Hospital.

No. 303. From the Inspector General, Medical Department, to the Secretary to Government, Revenue Department, dated Fort Saint George, 9th March 1867, No. 84.

1. In continuation of this Office letter No. 372, of 11th October 1866, I have the honor to forward, for submission to the Home Government, a copy of each of the tabulated reports received printed since that date, of the therapeutic effects of the Chinchona alkaloids received from England for experimental trial.

2. The Report and tabulated statistics, received up to the end of February by the Chinchona Commission, have already been submitted to Government.

LIST.

	Chincho-nine.	Chinchoni-dine.	Quinidine.	Chinchona leaves and bark.	Report.
Dr. Chipperfield, General Hospital, Madras	1	1	1	...	1
Dr. Cleveland, Mysore	1	1	1	...	...
Dr. Dougall, Northern Circars ..	2	2	2	...	...
Dr. Fitzgerald, Labuan	2	2	1	...	...
Dr. Foy, Sumbulpore	3	3	3	...	...
Dr. Heard, Shemogah	2	2	2	...	...
Dr. Henderson, Bangalore	...	1	1	...	...
Dr. Houston, Doomiguidiem ...	3	2	2	1	...
Dr. Keess, Goodaloor (Wynaad.)	3	3	3	1	1
Dr. Oswald, Mysore	...	...	2	1	...
Mr. Wade, Goodaloor (Wynaad.)	...	1	2	...	...
Dr. Walters, Secunderabad ...	3	3	2	3	...
Dr. White, Kamptee	1	...	1	...	...
Dr. Whitton, Cochin	2	1	2	1	1
Dr. Miller, Thyetmyoo	...	...	1	...	...

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19th March 1867.

No. 304. ORDER THEREON, 19th March 1867, No. 652.

Miscellaneous.

1. Ordered that these papers be transmitted to the Secretary of State.

2. This preliminary report of the Members of the Chinchona Commission on the results of the experimental use of the Chinchona alkaloids is very satisfactory and encouraging.

(True Extract.)

(Signed) W. HUDLESTON,
Secretary to Government.

To the President and Members of the Chinchona Commission.
,, the Principal Inspector General of the Medical Department.
,, the Superintendent Government Chinchona Plantations.
,, Mr. J. Broughton, Government Quinologist.

Pub. No. I. Suggestion.

10. We beg to direct attention to the tables, &c., in the Appendix. It gives us much pleasure in testifying that the experiments conducted by Dr. Keess at Goodaloor have been most carefully recorded.

11. Mr. Cornish, Secretary to the Principal Inspector General, in addition to his other duties, voluntarily undertook those of Secretary to the Commission. For the mode in which these duties have been carried out, the members of the Commission feel that their best acknowledgments are due to that gentleman.

MADRAS,
28th *February* 1867.

We have the honor to remain,
Sir,
Your obedient Servants,

President.

Members of the Chinchona Commission.

Revenue Department

No. 652.

Proceedings of the Madras Government

Under date the 19th March 1867.

Read the following Papers

From the Presidt. & Members of the Chinchona Commission.

Submitting a preliminary report of the proceedings to ascertain the result of the experimental use of Chinchona alkaloids and promising to forward more detailed observations when the results of the experiments still in progress are more fully known.

(Here enter 28th Feby. /67)

From the Inspr. Genl. Medl. Deptt.

Forwards tabulated reports of the Chinchona Alkaloids.

(Here enter 9th March 1867 No. 84)

Ordered that these papers be transmitted to the Secretary of State.

This preliminary report of the members of the Chinchona Commission on the results of the experimental use of the Chinchona alkaloids

is

Reported to England
D/ 25th March N:19 of 1867
Mis

Revenue 1867 Despatch
Pro of Govt for March

A·652

of the Madras Govt
dy 6 March 1867

Encr the Proceedings of the Chinchona Commr dated 18th April 1868 C Nº 1468.

Report of the Commissioner on the results of Experimental use of Chinchona Alkaloids, considered satisfactory. Mistranslation to Secretary of State, ordered.

A·302 to 304

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